BRITISH MEDICAL JOURNAL

LONDON SATURDAY JUNE 18 1960

THE BEGINNINGS OF THE NATIONAL HOSPITAL, QUEEN SQUARE (1859–1860)*

BY

MACDONALD CRITCHLEY, M.D., F.R.C.P., F.A.C.P.

Senior Physician, National Hospital, Queen Square, London

As a background to the story of the opening of the National Hospital in 1860, the state of medicine, as it existed in London during the first half of the nineteenth century, may be briefly surveyed with special attention to neurology. In many ways it was a dull if not an arid period. It has been called "the age of medical degradation," as marking the lowest ebb in medicine for centuries. Physicians had largely neglected the nervous system, its structure, function, and pathology. True, a century and a half before, Willis had made many promising observations; but these were clues which others had failed to pursue, and many indeed were forgotten.

At about the mid-point of the nineteenth century the up-and-coming fashionable doctors were Sir William Jenner (b. 1815) and Sir William Gull (b. 1816). The heyday of Sir Samuel Wilks came a little later. None of these men, however, can be said to have greatly advanced the knowledge of organic nervous disease. The Guy's galaxy of talent proved a little more fruitful. Richard Bright (b. 1789) had interested himself in apoplexy, and his writings upon this topic were full of substance even though the attainment was patchy. From Dublin one nervous disorder at least had been explored through the brilliance of Robert Graves (b. 1796).

Foundations of London Neurology

In London the principal exponent of the lush, but obscure, symptomatology of nervous disease was Robert Bentley Todd (b. 1809), physician to King's College Hospital. Todd must be looked upon as one of the first precursor-neurologists, for he enriched our knowledge with his observations upon lead palsy, and especially upon post-epileptic hemiplegia, which we still speak of as Todd's paralysis. To him is due the credit for the earliest description of tabes dorsalis, made four years before Romberg, eight years before Russell Reynolds, and 11 years before Duchenne, who is usually, but wrongly, accorded priority. Todd's untimely and unnecessary death from cirrhosis of the liver at the age of 50 was a considerable loss to medicine, and to neurology in particular. It could almost be said of him that, like the Persian philosopher, he had been in the habit of deliberating each problem twice over, first drunk and then sober; or perhaps it was the other way round. Had Todd survived another year or two he would surely have been invited to join the staff of the National Hospital. As it was, his pupil Julius Althaus founded in 1866 the London Infirmary for Epilepsy and Paralysis, afterwards known as the Maida Vale Hospital for Nervous Disorders.

The formative stage of neurology was also facilitated by work of an experimental character, carried out, as it so often was in those days, by part-time practitioners rather than by academic professionals. In this connexion Charles Bell (b. 1774) was pre-eminent. From his makeshift laboratories in Leicester Square and in Soho Square, and from the Hunters' old school of anatomy in Windmill Street, Bell gathered material for his *Essays on the Anatomy of Expression* (1806) and for his studies on the nature and function of the spinal roots (1810). Work upon the anatomy of the facial nerve and of the long thoracic nerve led to the publication of his book *The Nervous System of the Human Body* (1830). This was more than a simple anatomical atlas, for it contained illustrated accounts of morbid affections, later to be described more fully, such as Thomsen's disease and pseudo-hypertrophic muscular dystrophy. His final monograph was upon *The Hand* (1830), which he was commissioned to write by the Royal Society, supported by the Bridgewater Legacy.

Another great scientific figure of that time was the Nottingham physician, Marshall Hall (b. 1790). Moving to London at the age of 36, he became a tireless writer and researcher, though never lucky enough to attain the honour of a hospital appointment. His principal work was *The Reflex Function of the Medulla Oblongata and Medulla Spinalis* (1833). Although reflex action had already been envisaged by Descartes, by Boyle, and by Hales, it was Marshall Hall who really established this phenomenon as a cardinal property of the nervous system. Only tardily were his ideas accepted by his colleagues, put off perhaps by traits in his character or manner which were unattractive. Bentley Todd and Professor Carpenter opposed him: the Royal Society turned a deaf ear and refused to publish his writings. Abroad, he was acclaimed. In the City of York Thomas Laycock had, for one, realized the importance of Marshall Hall's work, and in due course he doubtless indoctrinated his pupils, Hughlings Jackson and David Ferrier.

Such, then, were the slender foundations of London neurology as it existed in 1860. Contributions from the Continent seeped in, it is true, but in a slow trickle. In Berlin, Romberg was 65 at the time of the birth of the National Hospital. Türck was 50, and Robert

*Based on an address given to the Osler Club on March 15, 1960.

Remak 45. Among French contributors, Magendie had died five years previously; Flourens was 66 and Claude Bernard 47, Cruveilhier had retired, being 69 years of age, while Baillarger was 51, Duchenne 54, Charcot 35, and Vulpian 34. Bouillaud, the Dean, was pontificating in Paris at the age of 64.

London at this time was therefore witnessing the false dawn of neurological science. Neurologists in the true sense of the word did not exist, and there were no neurological departments in any of the teaching hospitals. Epileptics and victims of paralysis lay in their own plight at home, if indeed they were not condemned to the semi-neglect of Poor Law hospitals and asylums for the insane.

Romberg's Work

Nor was neurological teaching the showpiece it was later to become. Even the literature of nervous disorder was sparse. Charles Bell had gone so far as to state that it would be a long time before combined efforts would enable a medical author to arrange and accurately describe the diseases of the nervous system. However, in 1840, M. H. Romberg endeavoured to do so. After asserting, in more sanguine vein, that "in no department of pathology had physiology exerted so great an influence, and that nowhere had free research achieved so glorious a victory over dull, traditional routine, as in the doctrine of nervous disease," he proceeded to issue the first part of his manual upon that subject. Dedicated to von Humboldt, the work was issued in serial form between 1840 and 1846. It was not until 1853, however, that E. H. Sieveking translated it into English.

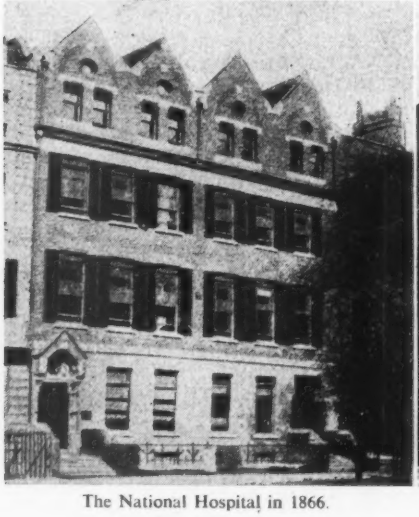
Even when judged by contemporary standards, much of this bulky work of Romberg's makes disappointing reading. He deserves great credit, however, for the way in which he based his study of disease upon the lessons of physiology. In view of the present-day cult of brain-chemistry it is interesting to find him issuing a warning against the tendency which was even at that time prevalent in Germany and elsewhere—"to seek for all explanations of diseased action exclusively either in the chemical changes occurring in the fluids and solids during life, or in the manifestations of morbid change as presented in the dead house."

Though this work is often referred to as the first textbook of neurology, this statement is not quite accurate, for a few other specialized writings were also available prior to 1840. James Parkinson's *Essay on the Shaking Palsy* was written in 1817, but it stands, of course, in a class all of its own as being a monograph. Special mention should be made of John Cooke's *Treatise in Nervous Diseases*, which was published in two volumes, in 1820 and 1823, respectively, but which is now almost forgotten. In discussing what had been written upon neurological topics we must not forget the second volume of Bright's *Reports of Medical Cases* (1831); nor yet Benjamin Travers's *Constitutional Irritation and the Pathology of the Nervous System* (1835). Of a very special character was Robert Carswell's *Illustrations of the Elementary Forms of Disease* (1838), wherein we discover the first depictment of the pathology of disseminated sclerosis, made while the author was still a medical student in Glasgow. All these works antedated Romberg. His manual was shortly followed by Marshall Hall's dissertation *On the Diseases and Derangements of the Nervous System* (1841). A little later—but still in the pre-Queen Square era—appeared the popular treatise by A. L. Foville (1844); the *Traité Pratique des Maladies Nerveuses* by C. M. S. Sandras (1851); and Bentley Todd's *Clinical Lectures*, the second volume of which was largely devoted to nervous disorders (1857).

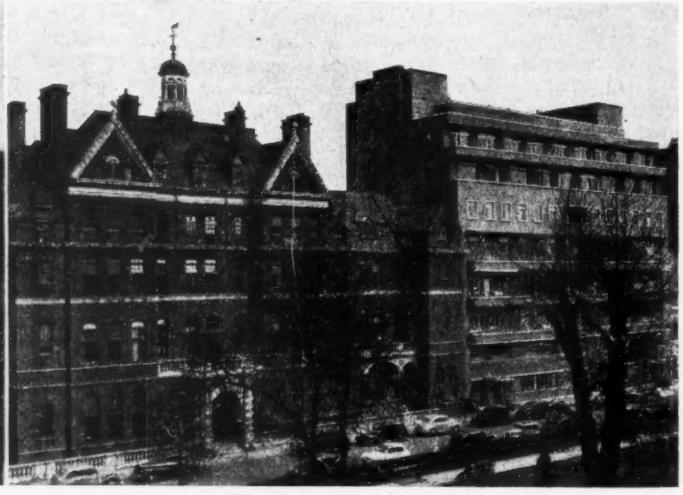
It was in such a climate of sciolism, coupled with lack of facilities for the care of the neurological sick and disabled, that our story opens.

Founders of the Hospital

In the Borough of St. Pancras, as it is now called, lived in modest circumstances a close-knit family comprising two sisters, Louisa and Johanna Chandler, and their brother Edward. A much-loved grandparent who had been responsible for their upbringing went into the country. She returned home paralysed, and remained so until her death. This serious illness drew attention to the utter lack of hospital provision and the inadequacy of specialist and nursing attention for such cases. The Chandlers were determined to correct these shortcomings, and from talks with their family doctor



The National Hospital in 1866.



The National Hospital in 1960.

they concluded that a special hospital was needed where victims of paralysis and also of epilepsy might receive humane and skilled investigation, management, and treatment. Undaunted by their slender resources, the Chandlers set out to interest their friends and to collect funds. The two sisters sold little trinket-boxes which they constructed from beads and cowrie shells, and by the end of two years they had collected the sum of £200. Of greater importance, they had also secured the sympathetic ear of the reigning Lord Mayor, Alderman David Wire, who himself had recently been afflicted with a hemiparesis.

Events now moved rapidly. A small working party formed itself, and a public meeting at the Mansion House was called for November 2, 1859. Here it was resolved to set up a special institution to be called the "Hospital for the Paralysed and Epileptic." A committee of management was formed, with the Lord Mayor as Chairman and Edward Chandler as Secretary. Suitable premises were sought, and early in 1860 an empty house was found and rented at No. 24, Queen Square. Its locality was suitable, and its size permitted an outdoor clinic, as well as accommodation for 10 in-patients.

A century ago Queen Square was steadily changing its character. Bloomsbury and Holborn had for many years been a favoured site for the town mansions of some of the nobility, which were set in open pastureland and marshes. Lamb's Conduit Fields was famed not only as a pleasance for city dwellers but also as a duelling-ground. At the end of the Stuart era the bracing air attracted wealthy invalids to settle here, and we find the ailing Duke of Gloucester, son of Queen Anne, building a house at what is now the southern aspect of Queen Square. To the north there was an attractive and uninterrupted view of Ken Woods and Highgate, and immediately in front was a streamlet which, taking origin in the spring at the Devil's Conduit, supplied with water the Christ's College in Newgate Street before joining the Fleet River. Retired East Indian merchants began to build near by in contemporary Old Gloucester Street and Boswell Street. In 1706 Sir Streynsham Martin, former Governor of Madras, was instrumental in founding the Church of St. George the Martyr close by. Gradually, from 1716 onwards, residences were built along the south, west, and east aspects of what was originally called Devonshire Square. It was afterwards renamed in honour of the reigning Queen Anne. The northern vistas were retained.

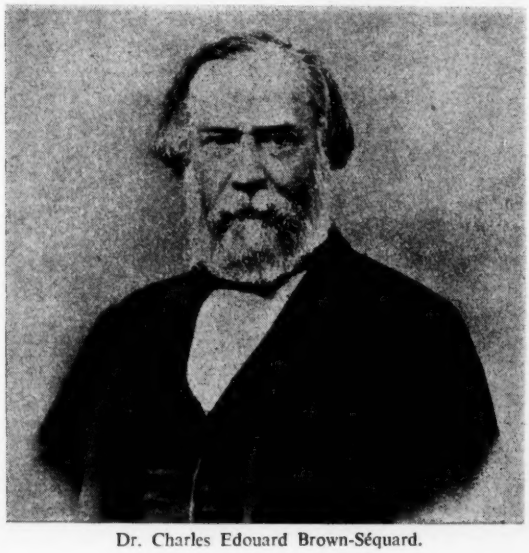
Queen Square became a fashionable locality popular with senior members of the Bench. Among the distinguished residents one may enumerate Dr. Campbell (friend of Dr. Johnson and Mrs. Thrale), Dr. Burney, Edmond Hoyle, Jonathan Richardson, Lord Chief Justice Denman, Mr. Sergeant Hanbury, Lord Chancellor Bathurst, Lord Chief Justice Pollock, and Elihu Yale.

During the mid-nineteenth century the Square became less modish but perhaps more interesting. The houses in Guilford Street had now cut off the view of the hills of Hampstead and Highgate. An expensive girls' school now appeared in the Square, and also the annexe to the Great Ormond Street College for Working Men. William Morris set up his workshop, office, and residence at No. 26. Miss Louisa Twining, the philanthropist, moved into what had been Dr. Campbell's residence at No. 20. St. Katherine's Convent was established at Nos. 32 and 33. The corner house, No. 1, became a tavern which took over the original title, "The Queen's Larder," Florence Nightingale instituted her St. John's Nursing Service in the Square, between the eventual Examination Hall on one side and the Alexandra Hip Hospital on the other. There was a time, too, when Queen Square showed signs of becoming a sort of Quartier Latin. Three taverns stood close by, patronized regularly by William Morris. The Square also contained, at one time or another, an antiquarian bookshop, Burr's Private Hotel, the town-house of a Gaiety girl, a spiritualist society, two doctors' surgeries, and even for a while a night-club. We recall, too, that in the eighteenth century two watchmen patrolled the Square by night to frighten away small boys and prowling harpies.

The National Hospital was the first of the various medical institutions which were later to find accommodation in the Square itself, though the Hospital for Sick Children had been founded a year or two before in Dr. Richard Mead's house close by in Great Ormond Street.

John Zachariah Laurence

The early fortunes of the National Hospital were considerably influenced by the support of four most unusual men. In the first place there was Dr. John Zachariah Laurence, born around 1829 in London. After graduating at University College Hospital he became a surgeon to the Farringdon Dispensary. Gradually his interests turned from surgery to ophthalmology, and in 1857 he helped to set up the South London Ophthalmic Hospital, now known as the Royal Eye Hospital. Two years later we find him joining the preliminary conferences instigated by the Chandler family, and, when at the Mansion House it was agreed to institute a special hospital for the paralysed and epileptic, Laurence became a member of the committee of management. In 1860, however, it was decided that a visiting surgeon should be elected to the National Hospital, and Laurence, desirous of this

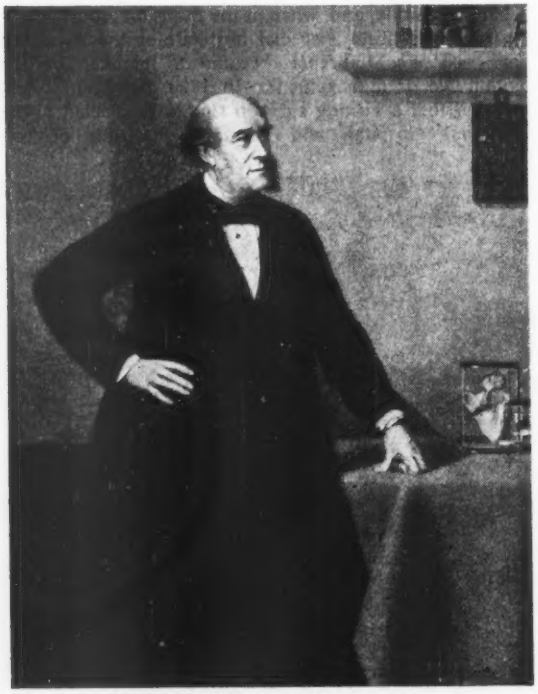


Dr. Charles Edouard Brown-Séquard.

appointment, resigned from the lay committee so as not to embarrass the selection board. Laurence was successful, but he did not hold the position longer than a year or two. His professional interests were becoming more and more optical. He edited the ophthalmic review, and he also became eye surgeon to St. Bartholomew's Hospital in Rochester. To-day Laurence's name is perpetuated in the so-called Laurence–Moon–Biedl syndrome. Laurence lived and practised at 30, Devonshire Street, and died in 1870. Of the Jewish Faith, Laurence was a man of great gifts and versatility, a philanthropist, and a pioneer of new ideas. He was also a fine linguist, and was deeply interested in the Arts.

Jabez Spence Ramskill

The second medical influence stemmed from Dr. Jabez Spence Ramskill, who was born in 1824 and educated at Guy's Hospital. He became a physician to the Metropolitan Free Hospital, and it is probable that about this time he became acquainted with the Chandler family. Almost certainly it was because of this friendship that Ramskill was made the first physician to the National Hospital, even before any actual accommodation had been secured. In the same year Ramskill was also elected assistant physician to the London Hospital, practising from St. Helen's Place, off Bishopsgate. Ramskill never became a top-ranking neurologist, though the students at the London are said to have greatly appreciated his lectures on the nervous system. He contributed articles to Reynold's Encyclopaedia of Medicine. Ramskill is said to have been deeply interested in the drug treatment of epilepsy, and when he died in 1897 he had unfortunately not completed an elaborate inquiry he had started into the problem 35 years before. It is strange that Ramskill was never elected a Fellow of the Royal College of Physicians, but he received the rarer tribute of being posthumously declared "a very genial and kindhearted man . . . greatly missed by his colleagues, and by his many friends outside the profession."



Sir William Fergusson.

Charles Edouard Brown-Séquard

The third medical personage who assisted at the birth of the National Hospital was a man of very different type—namely, the unpredictable Dr. Charles Edouard Brown-Séquard. Details of his strange career are well known. Born in 1817 in Mauritius of French-American parentage, Brown-Séquard carried out his medical studies in Paris. At an early age he showed interest in the physiology of the nervous system, and worked in the laboratories of Dr. Martin-Magron. While an extern on Dr. Trousseau's service he prosecuted researches, often using himself as a sort of experimental animal. When the coup d'état broke in December 1851, he deemed it expedient to leave France, and he settled for a while in Philadelphia. Here he did some of his best original work, including his well-known study of the effects of hemisection of the spinal cord. Incidentally, the familiar Brown-Séquard syndrome had already been demonstrated in 1700 by Ramazzini.

Brown-Séquard could never settle in contentment anywhere outside his beloved Paris, and, leaving Philadelphia, he married an American lady and then roughed it for a while in New York. Hopefully returning to Paris, he found no job available, and so proceeded to Mauritius to assist in controlling a cholera epidemic. In 1854 Brown-Séquard returned to America. His appointment at Richmond, Virginia, proved uncongenial and the facilities inadequate. Whispers went around that in his veins there ran a negroid streak. After a year he resigned and returned to Paris, for the death of Magendie had caused a vacancy at the Collège de France. Claude Bernard, however, was the successful applicant. In 1860 Brown-Séquard was invited to deliver in London a course of lectures at the Royal College of Surgeons. While in London he was approached—by whom we do not know—to join Ramskill as physician to the newly opened National Hospital, Queen Square.

Brown-Séquard enthusiastically agreed, and in a short while he prospered. Private patients flocked to him, while such honours as the Goulstonian Lectureship and the Fellowship of the Royal Society fell into his lap. He enjoyed his work at the National Hospital, and each week in the board-room he would hold clinical demonstrations which any medical man was welcome to attend. He set up house in No. 25 Cavendish Square, and he took under his wing young Dr. Victor Bazire, a fellow compatriot and later a colleague at the National Hospital.

Something went wrong, however. After four and a half years he resigned, and a little later he left London altogether. Perhaps it was because of the pressure of practice; perhaps it was because of his shattered health. Maybe it was the influence of his American wife that induced him to accept yet another disappointing job, a professorial chair at Harvard. Brown-Séquard's subsequent rovings do not concern us, for he did not return to London. Let us simply recall that eventually he realized his life's ambition: at 61 years he was

elected to the Collège de France. His latter-day researches were endocrinological, for he had outgrown the nervous system.

William Fergusson

The fourth man who influenced the fortunes of the National Hospital in its earliest days was the distinguished surgeon William Fergusson. Fifty-two years of age, he had left Edinburgh for King's College Hospital 20 years previously. Already his prestige was great, for he was Surgeon Extraordinary to the Queen, Surgeon in Ordinary to the Prince Consort, and later still Serjeant-Surgeon to Her Majesty. His Presidency of the Royal College of Surgeons and his baronetcy were a few years ahead. Fergusson's surgical repute lay in his technical expertness, for "he had the eye of an eagle, the heart of a lion, and the hand of a lady." Though a brilliant operator, he was better known for his judicious conservatism. He did not shine as a lecturer, largely owing to his reticence and his imperfect command over abstract subjects. He was a friendly, good-natured, and courteous man. Tall and handsome, the impact of his commanding presence was offset somewhat by a powerful East Lothian accent. Four years before the founding of the National Hospital he had been discreetly invited to visit Paris and attend the Emperor Napoleon III on account of a train of symptoms which, in retrospect, have a decidedly neurotic ring to them. Fergusson is remembered in yet another connexion. As a young anatomist in Edinburgh he had become acquainted with the notorious body-snatchers, Burke and Hare, at whose trial he was summoned to give evidence. Sir William Fergusson's acceptance of the invitation to serve as consulting surgeon to the National Hospital proved an invaluable asset, by endowing not only distinction but respectability to Queen Square.

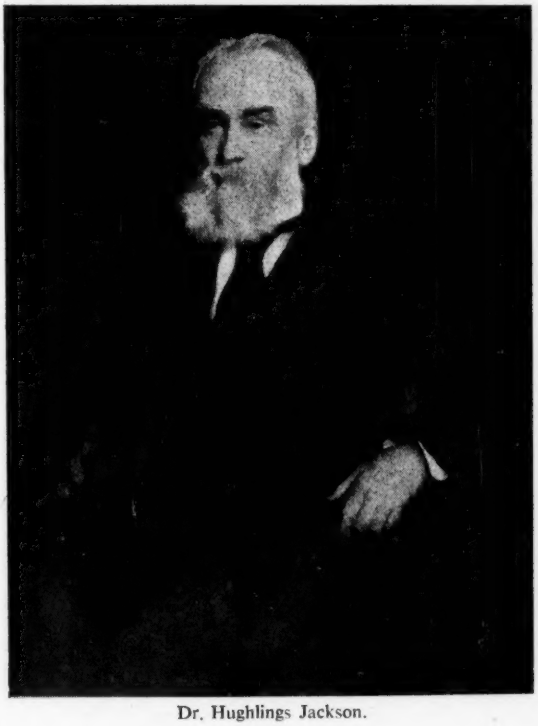
Innovations in the First Decade

During the first decade of its existence the National Hospital had grown in wealth, capacity, and prestige. From the start it showed itself something of an innovator in hospital management. Thus it was the first to institute day-rooms, to employ male nurses, and to make modest subsistence charges in suitable cases. From its beginnings the hospital took pride in its home-like cosy atmosphere. Though bickerings went on between the Board and its employees—not excepting the resident doctors—from the patient's standpoint it was a friendly hospital. As a pioneer in electrotherapy it became well known for its department of physical medicine. Thus we read in 1866: "the electrical room—a model of its kind—it is, we think, the only room of the sort in English hospitals." Two years later the *British Medical Journal* wrote: "To each ward is attached the usual day-room—an improvement introduced in England by this hospital and which is found to exercise a most beneficial effect on the health and comfort of the inmates. In each day-room is a library and everything is furnished in the homely and tasteful manner which characterizes this whole hospital . . . the baths consist of hot and cold plunge baths, shower, douche, sitz, needle, Russian and sulphur baths, and are arranged in a comfortable and thoughtful manner."

Even Thomas Wakley, the firebrand editor of the *Lancet*, who—like some medical reactionaries still—heartily disapproved of special hospitals in principle, had a kind word for Queen Square. "It cannot be doubted," the editor wrote, "that the principle of multiplying medical specialities is open to the serious objection that by favouring the isolated study of a particular disease, it tends to obscure the relations of pathology, and may thus even obstruct the knowledge of the very disease it is sought to advance. It is on this ground that we should oppose the establishment of any new hospital to be devoted to a special form of disease, unless a very strong and peculiar case of necessity were made out. We think no one can question that such a case exists for a special hospital for epileptics. . . . These were the views which, for several of the latter years of his useful life, occupied the sagacious mind of our great physiologist Dr. Marshall Hall. These views led him two years ago to propose the founding of a hospital for epileptics."

A more ambiguous note was struck by a visiting German physician who described the National Hospital as a "veritable jewel-box. The patients' rooms are furnished like the lounges of a first-class hotel, carpets, flowers, and pictures everywhere; everything is clean and elegant." He went on to say that one would search in vain here for bad epileptics or unclean paralytics, for such cases would certainly not be accepted. "The voluntary donors are well pleased with their beautiful work, but they are reluctant to have it disfigured and therefore steer clear of such elements whom they feel would tend to spoil their project."

There is also a reference to the National Hospital in *The Times* of 1873. "It differs from other special hospitals in owing its origin to no ambitious practitioner, and even to no medical instigation, but to the active and untiring benevolence of two ladies, who had witnessed, in a member of their own family, the suffering attendant

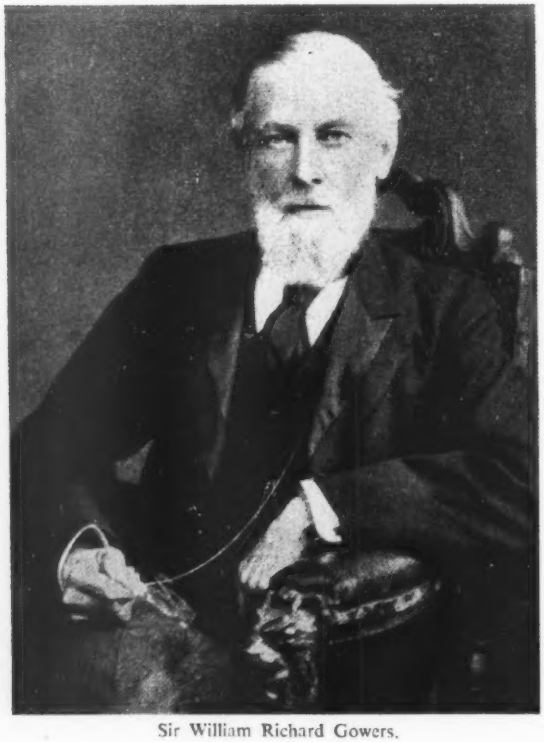


Dr. Hughlings Jackson.

upon paralysis, and who knew that the paralysed were admitted sparingly and with difficulty into general hospitals. It differs also in the number and eminence of the members of its medical staff, in the character of absolute publicity that attaches to all its proceedings, and in the general excellence of its management."

The academic reputation of a hospital does not depend upon fittings and furnishings. An international prestige is built upon the spirit of service within the wards, combined with a high level of teaching, of professional attainment, and of research. The National Hospital was indeed fortunate in its honorary staff. Men of outstanding ability—visionaries some of them; others of them patient observers—most of them brilliant teachers, such constituted the nineteenth-century staff. All were individualists and, as such, were occasionally at loggerheads, for mountain does not mingle with mountain. It would not be an exaggeration to say that of the leaders of the profession in the Victorian era many were honoraries at Queen Square.

From this company two stand out as supreme exponents—Hughlings Jackson and Sir William Gowers. Their place in the annals of the discipline of neurology is unquestioned. Very different in their personalities and achievement, they were complementary. Each held the other in high esteem. There were indeed certain common traits. Both came of humble parentage. Neither had the advantage of elaborate formal schooling, for they both finished at the age of 15. It would not be going too far to declare that both Jackson and Gowers were largely self-taught, in that they owed more to their personal exertions than to any schoolmaster. Both young men began their careers as apprentices to general practitioners. As graduates they both came under the influence of wise and experienced sponsors—Dr. Thomas Laycock and Sir William Jenner, respectively. Jackson, who was 10 years older than Gowers, became the first assistant physician to the National Hospital, while the other filled the first appointment as medical registrar. In this way they began their brilliant yet divergent careers in neurology.



Sir William Richard Gowers.

Both Gowers and Jackson were endowed with the same ability of close and accurate observation, combined with a sincerely honest method of recording. In most other professional respects, however, they differed.

Hughlings Jackson

Jackson is rightly regarded as the father of British neurology, for he inspired others by his thoughtful and interrogative attitude towards the problems of nervous function. Darwin had just published his *Origin of Species* when the National Hospital was founded in 1860, and exciting ideas were in the air. Herbert Spencer had coined the term "evolution." Jackson examined the notion in its possible bearing upon nervous function, and he was eventually led to a study of the phenomena of evolution and of dissolution within the nervous system. This doctrine was merely a single instance of Jackson's philosophic approach. It is not necessary to enumerate his many other important contributions, for they are well documented and well known. As might be expected, he was not acclaimed a pioneer at the time; he was, it must be confessed, not really comprehended even by his able colleagues. As Hazlitt has said, the chief disadvantage of knowing more and seeing more than others is to be not generally understood. Jackson seemed never to be addressing a contemporary audience. His ways of thinking became accepted only after a considerable interval, and then largely through the intermediary of such interpreters as Pick, Freud, Sittig, Head, and von Monakow. Neurologists, however, almost in spite of themselves, unwillingly became Jacksonians, and whatever we British exponents to-day possess in the way of a philosophy of neurology we owe mainly to Jackson.

Jackson himself was of course largely responsible for his intellectual isolation. Unlike most of his colleagues, he could not teach; neither could he write clearly or crisply. He did not attend medical meetings, for he was fidgety and quickly bored.

Though his work was not fully understood by his contemporaries, it was eventually realized that within their midst there was a genius. As Jackson grew older he found a secure place in the respect and even affection of his colleagues. He became a legend in his own lifetime.

Gowers

Gowers was different. Whereas Jackson was inclined to be untidy, and at times vague, Gowers was obsessional, perfectionist, and exacting. Equally astute as a clinician, Gowers recorded punctiliously. He had a collector's eye, for he could note, appraise, sort, and docket all of the neurological scene that went on around him. He was the supreme natural historian of disease. As I have said elsewhere, the neurological sick were to him like the flora of a tropical jungle, and his keen eye and his flair enabled him to identify, arrange, and classify. He learned to recognize the divers modifications of the banal or everyday material, while he quickly detected the rarities. To quote Moxon, he can be said to have known his diseases not only like a

zoologist would know his species and his genera and his orders, but as a hunter knows his lions and tigers.

Gowers possessed two other powerful assets. He was a magnificent teacher, whether demonstrating a case or delivering a set lecture. In the Victorian age of medicine news soon got around that the out-patient clinics at Queen Square were occasions not to be missed, especially when Gowers was in attendance. The other great accomplishment which Gowers possessed was a feeling for language and its proper employment. Both his lectures and his papers were couched in a most attractive and patrician style, yet austere and crystal-clear. So richly endowed, he brought out his *Manual of Diseases of the Nervous System* in two volumes, in 1886 and 1888 respectively. The *Manual* achieved an immediate ovation, as might be expected. Nothing like this work had been seen before; or has been seen since, for that matter. Gowers relied little upon the work of others, for all the subject-matter was garnered from his own case-notes and clinical experience. Even the illustrations were his own work, being drawings which he had made of his personal case-material. This book has affectionately but fittingly been termed the "Bible of Neurology," and there is still an axiom at Queen Square that no one who imagines he has stumbled upon something novel or obscure should neglect to consult the *Manual* before claiming originality or hurrying into print.

In 1871 Gowers, in his capacity as medical registrar, drew up the first nosological table recording the diagnoses of the in-patients at the hospital. This interesting list (see Table) has an almost modern appearance, and contrasts vividly with the neurological classification adopted by Romberg, with its emphasis on neuroses of motility, neuroses of sensibility, hyperaesthesiae, and spasms.

CEREBRAL PARALYSIS	
Hemiplegia, right	19
" left	9
Aphasia	2
NUCLEAR PARALYSIS	
Labio-glosso-laryngeal	2
Facial	1
TUMOURS OF BRAIN	4
SPINAL DISEASES	
Locomotor ataxy	4
PARAPLEGIAS	
Primary	22
Secondary to disease of vertebrae	4
SPINAL INFANTILE PARALYSIS	3
PROGRESSIVE MUSCULAR ATROPHY	2
Non-progressive muscular atrophy	2
DISSEMINATED PARALYSES	
Degenerative	1
Non-degenerative	4
TOXIC PARALYSES	
Diphtheritic	1
Lead palsy	5
PERIPHERAL PARALYSES	
Limbs	2
Face	1
EPILEPSY	65
Convulsions with chronic softening	1
Urinoemia	1
Local spasm	1
Chorea	5
Stammering	1
Cephalalgia	1
Neuralgia	1
	168

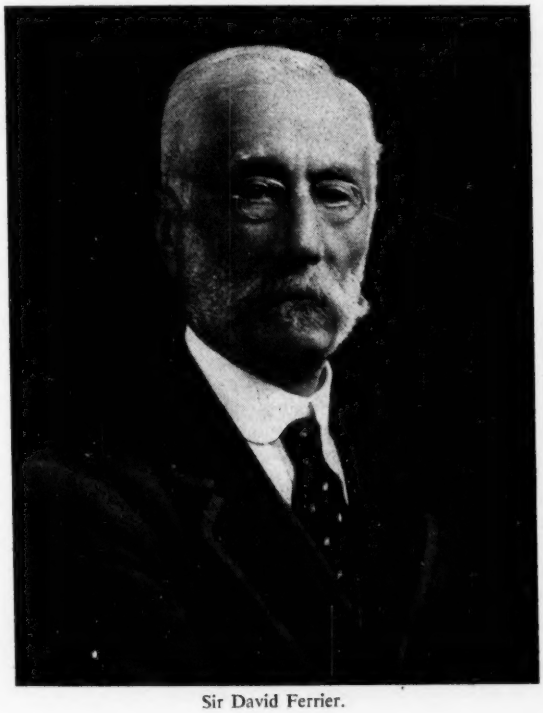
Jackson and Gowers were the benevolent Gog and Magog of the National Hospital, but there were other giants, too. Not far behind in brilliance and attainment were two other important figures, Victor Horsley and David Ferrier.

Ferrier and Horsley

David Ferrier was a perky and ambitious man of diminutive stature, who found his life-work only after one or two false starts. Psychology, general practice, forensic medicine, were for him the unlikely paths to neurophysiology. He was a clinician, too, and even secured a fashionable practice, but he was uneasy and undistinguished in that particular role. Again, he turned from one hospital to another until he settled at King's in 1874 and the National Hospital in 1880. Ferrier's great contribution lay in experimental physiology, and his researches were made at a particularly significant moment. They followed and confirmed the work which was being done in Germany, but, whereas Fritsch and Hitzig used one form of electrical stimulation of the cortex, Ferrier used another. The timing was also propitious in that Hughlings Jackson had propounded on theoretical grounds a conception of brain function which Ferrier was able to substantiate in the laboratory.

To Ferrier, too, credit is due in a rather unexpected way. He can be regarded as the inspirer of neurosurgery, for he repeatedly urged that certain morbid conditions of the brain were within the competency of surgical intervention. Over and over again he proclaimed that there was nothing sacred or untouchable about the coverings of the brain and that the dura was no more a barrier than the peritoneum. His beliefs were soon supported; for in 1884, at the Maida Vale Hospital, Rickman Godlee performed the first surgical removal of a growth from the brain. As a correspondent to *The Times* wrote shortly afterwards:

"It was not until Professor Ferrier had, by his experiments on animals, demonstrated the localization of sensory and motor functions in the cerebral

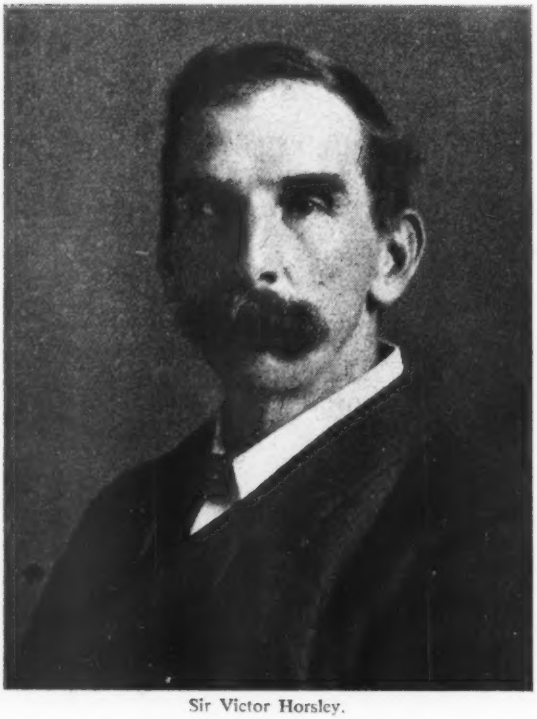


Sir David Ferrier.

hemispheres that the position of any diseased process by which they might be invaded could be definitely determined. . . . Dr. Hughes Bennet, under whose care the patient was, guided by Ferrier's experiments, skilfully interpreted the palsies and convulsive movements which the man exhibited, and deduced from them that a small tumour was lodged at one particular point in his 'dome of thought.' . . . Not more surely do the fidgetings of the electric needle intimate their origin and convey a meaning to the telegraph clerk than did the twitchings of this man's muscles announce that a tumour of limited dimensions was ensconsed at a particular point of a particular fold or convolution of the brain—the ascending frontal convolution of the right side."

Nor was this all. It was Ferrier, too, who realized that the appropriate treatment for intractable facial neuralgia was an ablation of the Gasserian ganglion, and it was he who persuaded his surgical colleague at King's, Mr. Rose, to perform this operation.

If Ferrier inspired neurosurgery, it was Victor Horsley who was its first grand executant. The recent centenary of this great man was the occasion for a considerable amount of appreciative writing, and repetition would be out of place. It is obvious from studying the biographical studies made by Paget, MacNalty, Jefferson, Sachs, and others that Horsley was something of a superman. Surgery aside, he would have attained pre-eminence whatever walk in life he had chosen. He combined a powerful drive with the habits of a cold perfectionist, and a crusading zeal which bordered on the fanatical. Perhaps his true métier would have been that of a dedicated politician, had it not been that an uncanny manual dexterity determined a career wherein art, science, and technique were combined.



Sir Victor Horsley.

Thereafter came a succession of notable physicians and surgeons to the National Hospital, but time will not permit me to do more than recite their names. Russell Reynolds (President of the R.C.P.); Thomas Buzzard, Crimea surgeon and close friend of Jackson; Charlton Bastian, erudite but dull; Beevor; Tooth; Batten, who, like Adie and Riddoch some years later, was to have his promising career prematurely terminated; James Taylor; the mercurial Risien Russell; Farquhar Buzzard, son of Thomas; and that complex figure who deserves a biography all to himself, Kinnier Wilson. Among the surgical and specialist staff there was Brudenall Carter, Marcus Gunn, and Leslie Paton as ophthalmic consultants; Felix Semon (courtier and man-about-town), Charles Ballance, Donald Armour, Percy Sargent, and, for a year or two, Hugh Cairns.

A Flourishing Medical School

For a hundred years the National Hospital has been famed for its teaching. Instruction in the board room by the original physicians was replaced by regular extempore teaching in the out-patient clinics, where picked men would be taken on as clinical assistants. Later still, ward rounds conducted by the full physicians became popular, and "clinical clerkships" became available to aspirants of a neurological career. These valuable appointments were much prized, and many of the leading neurologists of the world had at one time served as "clerks." In addition, set lectures were held from time to time; often they were published in the medical press. Gowers's famous address on pseudo-hypertrophic muscular dystrophy is a conspicuous example, and it actually constituted his first lecture at Queen Square. In the last century it was unusual to invite "guest lecturers": that practice did not become the vogue until after the last war. Within the first decade of its foundation, however, we find Dr. Duchenne on a visit to London, lecturing at the National Hospital.

By the turn of the century the National Hospital constituted a flourishing medical school, with a world-wide prestige. It operated, however, as a purely domestic concern, for it was not until the post-war reorganization of the University of London that it became an integral part of the British Postgraduate Medical Federation, and became known as "The Institute of Neurology."

Organic nervous disease lends itself to the teaching art, and certain among the staff became famous exponents. Gowers, the first of the great out-patient teachers, was followed by others, including that polished but unorthodox figure Risien Russell. It was he who excelled at making lightning diagnoses, the uncanny accuracy of which evoked astonishment among those who did not observe the sequence of clues nor emulate the rapid deductive thinking.

Two other names, though green in the memory of many physicians to-day, really belong to history. These were James Collier and Kinnier Wilson. Both were superb showmen in the best sense of the word. Both were endowed with an intellectual freshness which would often light up in a revealing fashion what had previously been a thing of obscurity. Unpredictable, both of them; originals, minor eccentrics, a little flamboyant. But whereas Collier was an enthusiastic man of affairs, Wilson was not. Collier attracted a local following rather than an international one; it was

otherwise with Wilson. Both wrote in an individual style, and what they had to impart was always important. Wilson's disciples formed a small band of votaries who would meet on a Saturday in the R.M.O.'s sitting-room to meditate upon the most puzzling clinical problems in the hospital. Wilson was a lone wolf, and if there were sections to be cut, photographs to be prepared, or recordings to be made, he would do the job himself. He gave the impression of aloofness except to those few who could penetrate his detachment.

Collier was different. Always approachable, he revelled in the admiration of the crowd. It was he who instituted the weekly clinical demonstrations which have become so famed. His technique of teaching was unconventional and even startling. He was easily seduced into tricks of hyperbole, when, as Oscar Wilde said, "facts fled before him like frightened forest things." In the lecture theatre Collier would resort to every device of display, eloquence, gesture, and emphasis. Overemphasis, too, was not despised. Collier would imitate a faulty articulation, or mimic an abnormal attitude, posture, or gait.

These were but a few of the great teachers at Queen Square. Some of them are still living. Others, prematurely deceased, are still remembered—like Adie and Riddoch, both of whom could hold an audience enrapt by their power of making simple sense out of intricate and confusing data. Listeners were shown a glimpse of the fascination which lies behind the art and science of neurology.

Sometimes it is asseverated darkly that "Queen Square is not what it used to be." First said in the 'eighties, it has been whispered consistently ever since. Doubtless it will still be murmured when the National Hospital is celebrating its second century.

The ninth annual statistical report to be published by the World Health Organization sets out in some 700 pages the demographic and health conditions of the countries of the world. It contains a number of innovations. In the first part, for instance, statistics of causes of death have been expanded. In the tables on causes of death figures have been given for deaths among young children by sex and by each year of age up to 4 years. Also a new table on the cause of infant mortality by age has been included. Among the other subjects which have been either expanded or newly introduced are cardiovascular diseases, malignant neoplasms, maternal mortality, and accidents according to the nature of injury. In the second part of the volume seasonal statistics of notifiable communicable diseases are given, with the distribution by sex and by age for certain of these diseases. The third part, which relates to statistics of health personnel, hospital establishments, and vaccinations, has also been rearranged and extended. A distinction is made between physicians proper and other practitioners entitled to provide treatment under particular and prescribed conditions in certain territories of Africa, Asia, and Oceania. The data also distinguish between private practitioners and physicians in the public health service. The number of inhabitants of each country or territory per physician is also given; the figures show vividly the still urgent need for medical personnel in certain areas of the world. Statistics of nurses and midwives have also been expanded. Statistics on vaccinations cover six major communicable diseases. An attempt has been made, for the first time, to give details of the population groups vaccinated and of the units to which the figures refer—i.e., primary vaccination or revaccination. (*Annual Epidemiological and Vital Statistics, 1956*, W.H.O., Geneva, 1959. Bilingual, French and English. H.M.S.O., P.O. Box 569, London, S.E.1, price £3.)

EXPIRATORY PRESSURES AND AIR FLOW DURING SPEECH

BY

M. H. DRAPER, Ph.D., M.B., B.S.

P. LADEFOGED, M.A.

AND

D. WHITTERIDGE, D.M., F.R.S.

From the Departments of Physiology and Phonetics, University of Edinburgh

All wind instruments require a suitable supply of air. For speech, this air is collected under pressure in the lungs and allowed to escape through the larynx and mouth in short bursts. Roos (1936) suggested that the muscles of the larynx, soft palate, and lips are the only mechanism for controlling this outflow of air, but there is evidence that the expiratory muscles provide not a steady expiratory pressure but varying pressure pulses (Stetson, 1951). By recording tracheal pressure and the electrical activity of the diaphragm and other respiratory muscles we have confirmed Stetson's view that expiratory muscles play a large part in producing the fluctuating pressures found in speech. We have made our measurements during the speech of normal persons and of patients with complete spinal transections.

Expiration during singing and the playing of wind instruments has been studied by Floyd and Silver (1950) and Campbell (1958). Buchthal (1959) has reviewed the recent work with similar electromyographic techniques on the activity of the laryngeal muscles during speech and singing. Some of the phonetic aspects of the present research have been discussed elsewhere (Ladefoged, Draper, and Whitteridge, 1958; Draper, Ladefoged, and Whitteridge, 1957, 1959).

Methods

In order to leave the mouth entirely free, the volume-changes in the chest were measured when the subject was standing in a body plethysmograph connected to a Krogh spirometer. The plethysmograph was made by welding together two 40-gallon (182-litre) steel drums and incorporating in the lid a yoke of sponge rubber as a neck seal.

Tracheal pressures were estimated from oesophageal pressures, recorded from a small latex balloon, about 1.5 cm. in diameter and 2.5 cm. long, sealed to the end of a "polythene" catheter of 2 mm. bore. The balloon was passed through the nose until it lay about 34 cm. from the external nares. Radiological examination showed that this corresponded approximately to the level of the bifurcation of the trachea in subjects about 1.8 m. in height. The balloon in the oesophagus was filled with 2 ml. of air and, as can be seen in Fig. 1, an approximate sphere of air was held between the thin posterior membrane of the trachea and the vertebral column. Thus any changes of pressure in the trachea can be transmitted to the air in the inflated balloon. The catheter was connected to a rubber tambour, and records of the membrane excursion were

obtained on a kymograph via a lever system and capillary pen. The excursions of the spirometer were recorded on the same kymograph. Howell and Peckett (1957) and Opie, Spalding, and Stott (1959) used a balloon 10 cm. long sited lower in the oesophagus to give a measure of intrapleural pressure; as discussed below, the size of the balloon and its position in the oesophagus are important.

Oesophageal and Tracheal Pressures

Experiments were carried out to check the validity of taking oesophageal pressure changes as a measure of tracheal pressure changes. First, a direct comparison was made in one subject. Tracheal pressure was recorded from a needle, 1.5-mm. bore, passed between the third and fourth tracheal rings in the midline. Pressures were measured during utterances such as counting from one to thirty or repeating "ma." Fig. 2 (open circles) shows the result. At pressures up to 12-cm. of water the correlation between oesophageal pressure and tracheal pressure during a sustained utterance of constant loudness is good.

In the second set of experiments three subjects with a balloon in the oesophagus exhaled steadily against a constant resistance. The pressure was measured by a side tube between the subject and the resistance. Fig. 2 (full circles) shows the mouth pressure and oesophageal pressure in the same subject at various levels of air-flow. The mouth pressure should be the same as that in the trachea if the air-flow is slow and there are no constrictions within the vocal tract or at the glottis. Such constrictions would be indicated by noise. As can be seen, the correlation between mouth pressure and oesophageal pressure is good.

A third series of experiments indicated that the size and position of the balloon in the oesophagus are important. Towards the end of a complete expiration, and thus beyond the expiratory excursions used in normal speech, there is frequently a tendency for oesophageal pressure to increase. At this time, in order to push out the small amount of air left in the lungs at the required pressure demanded by the loudness of the utterance (discussed below), most of the muscles of the thorax, abdomen, neck, and shoulder-girdle will be in action. Thus the balloon can now be influenced by such factors as the pushing up of the relaxed diaphragm by the greatly increased abdominal pressure and the descent of the larynx towards the thorax by the action of the neck muscles in maximum expiratory efforts. These effects were studied by recording the pressure changes during utterances with the balloon both high in the oesophagus where neck muscle influences predominate, and low in the oesophagus where abdominal and other influences should exert effects.

Fig. 1 shows the pressure changes seen when the balloon is in different positions in the oesophagus during an utterance such as counting, in a conversational voice, from one to thirty or reiterating "ma" for as long as a controlled loudness is possible. At each level the initial pressure changes are much the same, but as expiration proceeds the records from both the upper and the lower oesophagus show systematic increases which do not appear in the records from the central oesophagus. These increases in pressure can also be affected by movements such as bearing down in expiration or altering the quality of the voice by pulling the larynx up and down with the muscles of the neck.

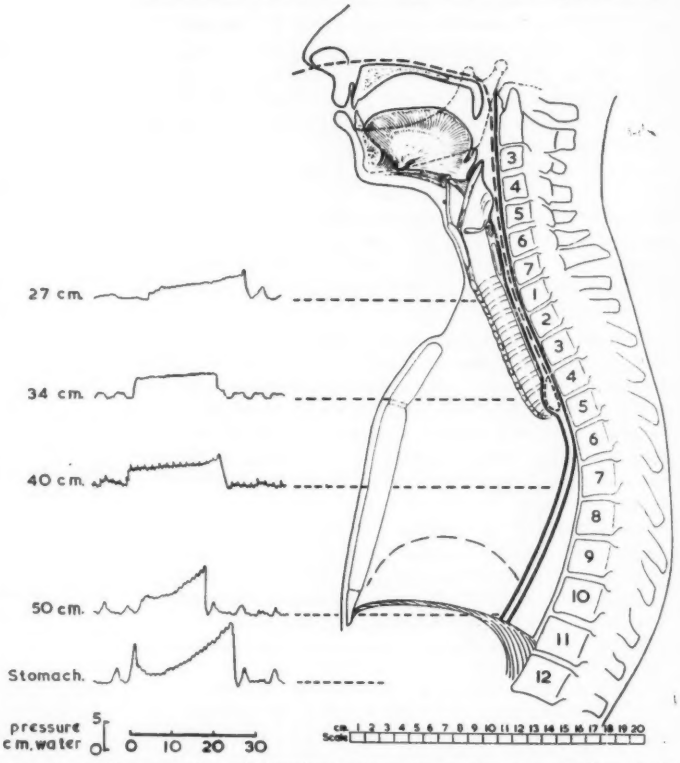


FIG. 1.—A diagrammatic scale-drawing to show the position of the balloon in the oesophagus when studying tracheal pressure changes. The bulge of the anterior aspect of the balloon into the thin posterior tracheal membrane has been slightly exaggerated for clarity. The broken line above the diaphragm represents the possible extreme position of the lateral parts of the diaphragm in deep expiration. At the side of the drawing are placed the pressure records obtained during a standard utterance at the levels 27, 34, 40, and 50 cm. from the external nares, and from the stomach (60 cm. down). The 34-cm. level gives the best indication of tracheal pressure changes and, as can be seen, is least influenced by other pressure changes, which become particularly prominent towards the end of a long utterance. (Time scale in seconds.)

These three sets of experiments show that the pressure changes in the trachea can be assessed with reasonable accuracy from measurements of pressure changes in a small balloon in the oesophagus.

The peristaltic contractions of the oesophagus are quite characteristic and easily distinguished from the changes caused by speech. There are also on occasion much slower changes in oesophageal tone which, unless measured against a constant baseline, may be overlooked, but as the pressure changes in speech in these experiments were large and rapid compared with these slow changes little difficulty in interpretation was encountered.

Electromyographic recordings were obtained using surface or concentric needle electrodes and the conventional cathode-ray oscillographic technique. Two double-beam cathode-ray tubes were used so that

four events could be photographed simultaneously. The surface electrodes consisted of small silver disks 0.8 cm. in diameter. Records obtained from surface electrodes rarely have a simple interpretation because of the complex nature of the muscle layers about the thorax and abdomen. They were useful over the rectus abdominis and over the scapular triangle, where the external intercostals can be studied. For recording the activity of the diaphragmatic crura, modified surface electrodes consisting of three circles of silver wire 0.5 cm. apart, one of which was earthed, wrapped around the end of a polythene catheter, were most satisfactory. This catheter was passed down the oesophagus until it rested between the crura of the diaphragm.

The greatest electrical activity occurred at about 50 cm. ± 1 cm. down from the external nares, in a subject 1.8 m. in height. The concentric needle electrodes used consisted of either a single insulated wire sealed in a varnished hypodermic needle or two 50-μ insulated silver wires sealed in a hypodermic needle with the tip of the needle ground down under binocular vision to expose the silver wires.

Two microphones were placed about 25 cm. in front of the subject's mouth. The output of one was fed into a high-quality tape recorder and a meter for measuring average signal strength. The output of the other was suitably amplified and displayed on one beam of the four-channel cathode-ray oscilloscope. Two channels were used for the electromyograms and the other for either pressure or volume changes.

Speech and Tracheal Pressure

Conversational speech with its hesitations and stresses is not easily analysed. As a standard utterance, a repetition of the single syllable "ma" at about 2 per sec. or counting up to thirty proved to be quite satisfactory. Fig. 3 shows the result of asking a resting subject to take a breath and to count for as long as possible at a conversational level of loudness. During quiet respiration the changes in oesophageal pressure are very small. When the subject breathes in more deeply the oesophageal pressure drops slightly, and when he begins to talk the pressure rises sharply to 3.5 cm. of water and the mean pressure remains at this level. At the same time the steady change in thoracic volume indicates that the mean flow of air through the upper air passages is also constant. At the end of the utterance, which is close to the limit of expiratory effort, the pressure drops and reverts to the resting pattern

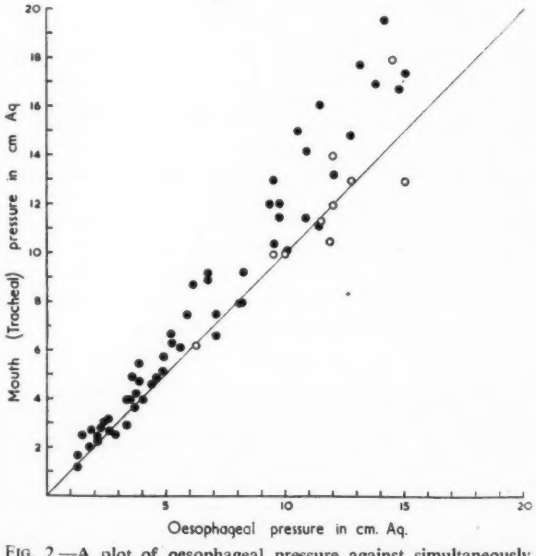


FIG. 2.—A plot of oesophageal pressure against simultaneously measured tracheal pressure (open circles) or mouth pressure (full circles). The measurements were made during sustained speech in the tracheal puncture experiment or during sustained exhalation against a constant resistance in the mouth pressure experiments. The full line is drawn at 45 degrees.

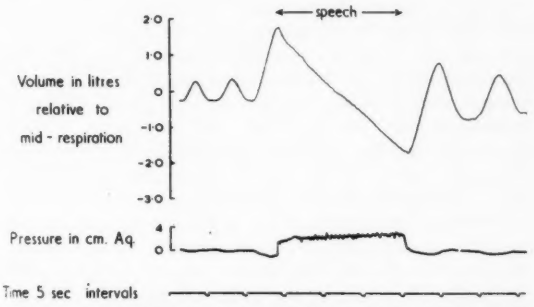


FIG. 3.—A simultaneous record of lung volume changes (top) measured from a body plethysmograph and tracheal pressure changes measured from an oesophageal balloon during normal breathing followed by a prolonged conversational utterance after a moderately deep breath. The small fluctuations in the mean pressure correspond to the stresses in the utterance, which was counting from one to 30.

If the loudness is increased, then the same pattern of changes is seen with a corresponding increase of air-flow and mean oesophageal pressure. It was not possible to measure the loudness in absolute terms in these experiments, which were conducted in an ordinary reverberant room. However, the intensity meter connected to one of the microphones showed that a change of 2 db in the intensity of the vowel in "ma" could be correlated with a change of the order of 1 cm. of water in the mean pressure level over the range of 40 db change and 20 cm. of water pressure in the trachea. Quiet talking usually occurred with a pressure of 4–6 cm. of water, and parade-ground shouting 40 db up in intensity level needed pressures between 20 and 30 cm. of water.

From these results it is clear that the louder the speech the higher the pressure in the trachea. The flow of air resulting depends on the setting of the vocal apparatus. If the loudness is kept constant, then the mean pressure in the trachea will also remain constant, despite the fact that the thoracic volume can change from maximum inspiration to maximum expiration. Superimposed on the mean pressure in the trachea, small fluctuations in pressure corresponding to stressed syllables in the utterance can often be seen. When a pressure-recording system with a faster time-constant is used (Ladefoged *et al.*, 1958), these smaller fluctuations become more obvious.

Muscular Control of Mean Tracheal Pressure

The next part of the investigation concerned itself with the development and maintenance of the

background pressure in the trachea and any muscular control of the superimposed fluctuations of pressure associated with stresses in speech. In three subjects simultaneous measurements were made of mid-oesophageal pressure, lung-volume changes, and electrical activity in two muscles concerned with respiration while uttering "ma" at different loudnesses and with lung-volume changes of about 4 litres. The external and internal intercostals, the diaphragm, the lattissimus dorsi, the rectus abdominis, and the external oblique were studied in pairs in each subject. The most convenient site for inserting the concentric needle electrodes for the internal intercostals was the fifth intercostal space 7.5 cm. posterior to the mid-axillary line. The needle can also be sited between the internal and external intercostals at this point. Sometimes it was desirable to have the electrode sampling unequivocally the activity of one intercostal muscle. The fourth interspace 7.5 cm. from the mid-sternum was found to be a suitable site for the internal intercostal alone as the external intercostals are deficient anteriorly. Likewise, the internal intercostals are deficient posteriorly, and in the region of the scapular triangle records were obtained which were undoubtedly from the external intercostals.

The results of such a study from one subject are set out in Fig. 4. To avoid confusion the activity of the external and internal intercostals has been set out in Fig. 4 I and the corresponding activity in the latissimus dorsi, rectus abdominis, and external oblique in Fig. 4 II. The symbols—that is, filled or open circle, and cross—indicate the point where, at the corresponding lung volume, the muscle activity stopped or started at the particular loudness under investigation. The dotted or full line indicates that the muscle was active. Thus in Fig. 4, consider an utterance at conversational loudness which would correspond to a pressure of 4 cm. of water. At the top of inspiration (2 litres above mid-respiration in these experiments) and the beginning of the speech, the inspiratory external intercostals are active and are needed to offset the passive recoil of the thorax and lungs. They stay active until the lung volume has declined to about 400 ml. above mid-respiration, when units start to drop out and units of the internal intercostal start to come in; at about 100 ml. above mid-respiration all external intercostal activity has ceased and the expiratory internal intercostal activity has taken over. At lower lung volumes the passive recoil is not sufficient alone to sustain the pressure of the air in the trachea at a constant level, and so expiratory muscles must become increasingly active as the lung volume decreases. Transferring to Fig. 4 II at the same pressure (4 cm. of water) it can be seen that as expiration deepens more muscle groups come in, latissimus dorsi appearing at about 1,300 ml. below mid-respiration.

If a much louder utterance is studied, say at 10 cm. of water, the external intercostals cease activity at about 1,200 ml. above mid-respiration and the expiratory groups of muscles come in at correspondingly earlier points in expiration. The point at which inspiratory muscles become silent while the expiratory muscles come into action at a given sustained positive tracheal pressure should occur on the relaxation curve. The two diagonal lines on the figures represent the passive recoil pressure range that might be expected at each lung volume, and are taken from the data of Howell and Peckett (1957). The top line corresponds to the average thoracic pressure–volume relationship in conscious supine subjects and the lower line corresponds to the relationship in the same group of anaesthetized and curarized subjects. The lung compliance corresponding to the top line is 0.15 l./cm. of water, and corresponds to the lower limit given for males, average age 28 years, in the tabulations of Dittmer and Grebe (1958). The

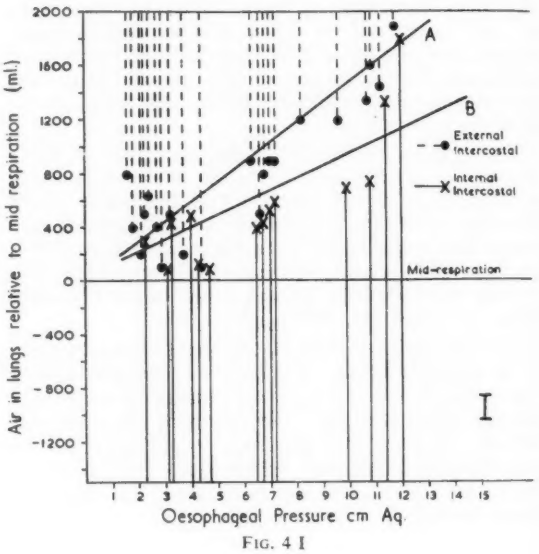


FIG. 4 I

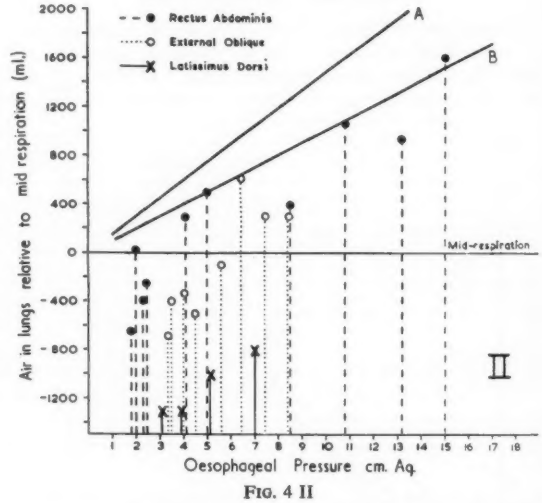


FIG. 4 II

FIG. 4 I and II.—Diagrams to show the changing muscular forces necessary to expel air from the lungs at different sustained pressures. 4 I is concerned with the internal and external intercostal muscles. 4 II shows separately, for convenience, the corresponding activity in the rectus abdominis, external oblique, and latissimus dorsi. In 4 I, at a conversational level of 4 cm. of water in the trachea, the external intercostal muscles are active until the chest volume is just above mid-respiration. Below this, with some overlap, the internal intercostals come into operation. In 4 II, as the chest volume decreases, the rectus abdominis, then the external oblique, and, finally, at the end of full expiration, the latissimus dorsi come into operation. At higher pressures the external intercostal muscles go out of action earlier and the other muscles come in earlier. The diagonal lines A and B are possible upper and lower limits of the relaxation pressure curve derived from Howell and Peckett (1957).

equivalent compliance of the lower line is 0.10 l./cm. of water and should represent the lower limit of compliance.

Howell and Peckett suggest that one of the possible factors for the reduction in the compliance in unconscious paralysed subjects is the absence of inspiratory muscle activity, which is very difficult to suppress by voluntary efforts when lung compliances are measured in conscious subjects. Thus it can reasonably be argued that the true compliance should lie between these two lines. Thoracic compliances were not measured in the subjects of these experiments and hence not too much weight can be placed on the derived lines of Fig. 4. However, it is clear that the cross-over between inspiratory and expiratory muscle groups at different pressures does occur along a line which gives a relaxation curve of the general slope to be expected from the data in the literature (see Dittmer and Grebe, 1958).

The observations in Fig. 4 are sufficient to give a clear idea of the general pattern. The points indicating the end of activity are not particularly consistent, apart from a general trend to come in or go out earlier as the pressure required rises in the trachea. It would need many hundreds of observations to define more clearly the pressure-volume range of each muscle group. Each point represents the cessation of activity in a few motor units, and if it falls short of the expected line it is probably because these particular units are recruited rather late in the general development of tension and hence go out of activity earlier.

The diaphragmatic activity is best considered separately because of its interest in connexion with beliefs concerning breath control, particularly in singing (see Luchsinger, 1953). In 9 out of 11 subjects the diaphragmatic activity ceased during the first two or three seconds of an utterance after a maximal inspiration, and thus played no part in the subsequent control of the thoracic volume. However, in two subjects the diaphragm did not relax for a considerable time, and there was increased activity of the expiratory muscles apparently to overcome the prolonged inspiratory activity. The diaphragmatic activity in expiration is what would be expected in the *Atemstütze* or "breath hold" concept of the mechanism for expiratory control (see Draper *et al.*, 1959). The present studies, so far as they go, indicate that in most people expiratory control during speech is primarily a matter of co-ordination between the external and internal intercostal muscles.

Speech in Paraplegic Subjects

The investigations described above show that the production of sustained speech depends upon the ability to produce a sustained positive pressure in the trachea by means of the activity of thoracic and abdominal muscles. Speech should be disturbed if these muscles are paralysed, so a number of paraplegics with lesions in the cord at levels ranging from C 4 to T 12 were examined. Because of their reduced vital capacity, patients with lesions between C 4 and C 8 could not produce long sentences. Most of them had only a limited amount of control of the pressure of the air in the lungs, and could not produce any increase in pressure when near the lower limit of their vital capacity. Consequently they were unable to stress the last word in a sentence such as "Please pass the *salt*." But they could all vary the degree of stress on the first few words of an utterance. Many of them had noticed their inability to "talk loudly" since their accident; and most of them had found that it was easier to talk when lying down.

The maximum pressures which can be maintained by paraplegics with lesions at different levels are indicative of the forces which various muscles can contribute to an expiratory effort. These pressures were recorded, and are as shown in Fig. 5.

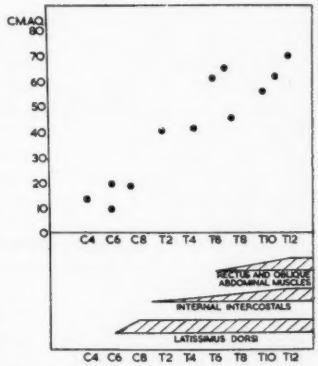


FIG. 5.—Observations of the maximum pressures which were maintained by paraplegic subjects with lesions at different levels. The damage to the principal expiratory muscles can be assessed in each subject from the segmental innervation diagram in the lower part of the figure.

It was striking that patients with lesions at C 8 to T 1 used the latissimus dorsi largely for talking. It could easily be felt contracting to produce stressed syllables. In patients with lesions at C 6 and C 5 this muscle was paralysed, but some expiratory pressure could be produced by adducting the scapulae with the levators and perhaps with the rhomboids.

Internal Intercostal Activity and Particulate Speech

Perhaps the most surprising observations made in this study were those concerning the activity of the internal intercostal muscles during speech and the correlation of this activity with the small changes in pressure seen superimposed on the mean tracheal pressure and the correspondence of these changes in turn with the production of certain elements of the utterance or the stresses in the utterance (Ladefoged *et al.*, 1958; Draper *et al.*, 1959). During quiet respiration there was usually no activity in the internal intercostals, but as soon as any utterance was attempted the internal intercostal muscles became active. Fig. 6, first utterance, shows that about 50 msec. before the speech begins—that is, before any detectable activity is seen in the microphone record—the motor units start activity, and this activity can be seen to fluctuate during the phrase, "He wanted to be an elevator operator." Study of short sentences such as this has shown a relationship between the action potential frequency and the stressed syllables or those elements, such as "h," which need more air flow. These correlations are not exact, probably because the motor-unit sample is too small to be fully representative. There are in the records of Fig. 6 perhaps up to 20 motor units active during the phrase. The fact that such a small sample taken from the whole chest wall can reflect to any degree the rapid changes occurring in speech is indicative that the intercostal muscles must be comparable in speed of action with the small muscles of the hand.

Fig. 6 shows how, as the phrase is repeated with the same breath, the total number of action potentials during the phrase increases as more and more energy

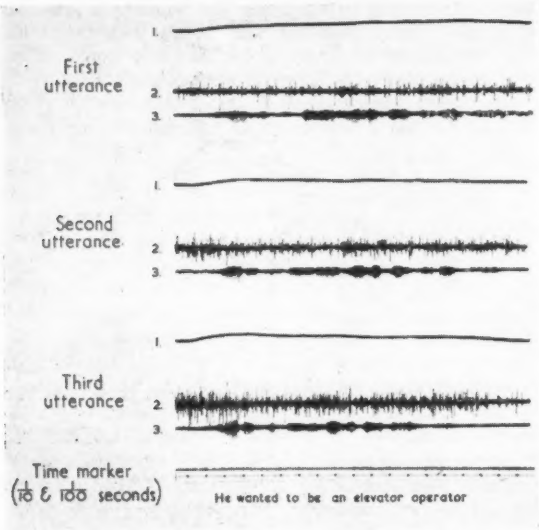


FIG. 6.—Activity recorded from the internal intercostal muscles during one breath and three successive repetitions of the phrase, "He wanted to be an elevator operator." The overall muscular activity increases as the chest volume decreases. Close examination of the records shows that in each utterance there is a consistent pulsing action of the muscle before stresses in the sentence. Line 1, oesophageal pressure; line 2, electromyogram of the internal intercostal muscle; line 3, microphone record.

must be expended to push out the air at constant mean pressure. The relationship between the moments of comparatively high muscular activity and certain elements of the utterance is preserved.

The activity of the internal intercostals during speech was consistently observed not only many times in the same subject but in all six subjects in whom electromyographic studies were carried out with concentric needle electrodes. This rapid variation of muscle activity was, with one exception, not observed in the other muscles examined in Fig. 4. Thus in this respect they are accessory muscles primarily concerned with the cruder aspects of the mean pressure level in the trachea. Pulsing can be achieved by these muscles if the speech effort is vigorous enough. Fig. 4 shows that at quiet conversational pressures (about 4 cm. of water) taking place within the normal tidal air (± 250 ml.) the only expiratory muscle operating is the internal intercostal. The rectus abdominis can come in early, but, contrary to phonetic belief, it does not appear to be concerned intimately with the production of the elements of speech; rather, its function would seem to be fixation of the anterior abdominal wall, usually coming in earlier than the external oblique. Thus the "squeeze" of the internal intercostals operates from the fixed first rib across each rib and then via the abdominal muscles to the pubic symphysis, Poupart's ligament, and crest of the ilium.

The exception mentioned earlier is in the action of the external intercostals. In one subject out of the three studied, activity was observed after the stressed syllable, thus checking the expulsion of air by the elastic recoil of the thorax. This checking action was seen only in utterances with lung volumes well above mid-respiration (Fig. 4 I).

The fact that bursts of action potentials are consistently observed in the internal intercostal muscles before stressed and certain other syllables—for example, those beginning with "h"—prompted a few observations on the general timing of this complicated mechanism. Simultaneous records were obtained of the activity of the internal intercostals, the oesophageal pressure, and the sound waves of a subject who was instructed to respond by saying "ma" as quickly as possible after hearing a stimulus such as a tap with a coin on the microphone. A typical record is reproduced in Fig. 7. The overall reaction-time varied considerably, as is to be expected in an unrehearsed subject. The shortest time from the start of the stimulus to the start of the internal intercostal activity was 140 msec.; the longest record was 320 msec. However, the interval between the beginning of internal intercostal muscle activity and the first sound was comparatively constant at 48 msec. for "ma," "me" and "nine" (S.D. 8; n=9). At 20–40 msec. after the muscle activity started the oesophageal pressure began to increase. Some further observations were made where the subject had simply to decide what utterance was required. He was then asked to repeat the number called. The time from the action potentials in the internal intercostals to the first sound was still constant at about 50 msec.

Wind Instruments

The pressures required for playing musical instruments have been reported previously (Roos, 1936). Sharpey-Schafer's and our results agree closely with the figures given (see Faulkner and Sharpey-Schafer, 1959). In flute-playing the problem in soft passages is to keep a steady pressure of 0.5 cm. of water—much lower than is usual in speech. If considerable inspiratory volume is taken and held, the problem is to oppose steadily the considerable recoil pressure exerted by the inflated chest. In oboe-playing, and particularly in trumpet-playing, the problem is to obtain the very high sustained intrathoracic pressures of up to 100 or even 160 mm. Hg. In Professor Faulkner, of Santa Barbara, who kindly acted as a subject, considerable activity was observed in the abdominal muscles, especially the external obliques, as soon as he began to play. Some activity was seen even during the inspiration preceding the playing.

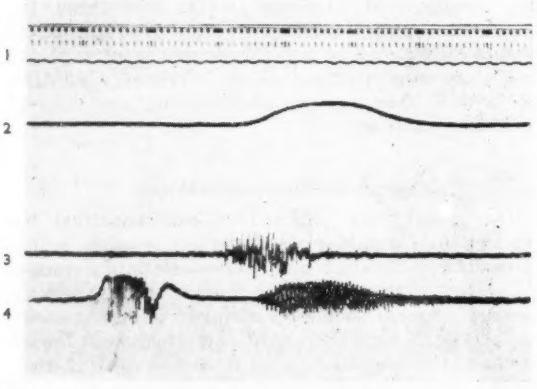


FIG. 7.—Simultaneous records of the sound waves of a stimulus and utterance (line 4), the activity in an internal intercostal muscle (line 3), and the oesophageal (i.e., tracheal) pressure change (line 2) in a subject instructed to say "ma" on hearing a tap on the microphone. The muscular activity precedes the beginning of the pressure wave by about 30 msec. and the sound waves by about 50 msec. Line 1 gives time marks in hundredths and tenths of seconds.

Diaphragmatic activity dropped to a minimum during the first second of expiration. With loud trumpet-playing, the recorded activity with diaphragmatic leads slowly increased again towards the end of expiration, but activity was always much less than that recorded during inspiration.

In view of the anatomical relationships of the oesophagus as it passes through the diaphragm, it seems unlikely that these action potentials can be ascribed to any other muscles. The activity in the external obliques increased steadily throughout expiration. The late re-entry of diaphragmatic activity in these extreme conditions is puzzling and no adequate explanation is available. This combination of contraction of abdominal muscles and diaphragm was also seen during efforts at "bearing down."

Summary

Methods are described for estimating the tracheal pressure during speech and of recording activity in the diaphragm and a variety of thoracic and abdominal muscles.

During a steady level of loudness of speech the mean tracheal pressure is kept remarkably steady. The pressure needed varies from 2 cm. of water for very quiet speech to 30 cm. for parade-ground shouting.

To attain a steady level of 2 cm. of water throughout an expiration the inspiratory muscles—the external intercostals—at first oppose the relaxation pressure (there is usually a short period when all muscles are inactive and the relaxation pressure acts alone); then expiratory muscles, beginning with the internal intercostals and later involving other muscles, such as the rectus abdominis, reinforce the diminishing relaxation pressure.

In paraplegics the maximal expiratory pressure that can be exerted is lower the higher the level of transection between T 12 and C 6.

The shortest reaction time when a subject was instructed to say "ma" as soon as possible after a sound was 140 msec. to the start of internal intercostal muscle activity. The first sound started consistently about 50 msec. later.

We are indebted to Dr. Ludwig Guttman for permission to examine some of his paraplegic patients. We thank Mr. C. Shepley, department of medical illustration, University of Edinburgh, for his assistance with Fig. 1, and Mr. W. T. S. Austin for his technical assistance throughout this study.

REFERENCES

Buchthal, F. (1959). *Quart. J. exp. Physiol.*, **44**, 137.
Campbell, E. J. M. (1958). *The Respiratory Muscles and the Mechanics of Breathing*. Lloyd-Luke, London.
Dittmer, D. S., and Grebe, R. M. (1958). *Handbook of Respiration*. Saunders, Philadelphia and London.
Draper, M. H., Ladefoged, P., and Whitteridge, D. (1957). *J. Physiol. (Lond.)*, **138**, 17P.
—— —— —— (1959). *J. Speech Res.*, **2**, 16.
Faulkner, M., and Sharpey-Schafer, E. P. (1959). *Brit. med. J.*, **1**, 685.
Floyd, W. F., and Silver, P. H. S. (1950). *J. Anat. (Lond.)*, **84**, 132.
Howell, J. B. L., and Peckett, B. W. (1957). *J. Physiol. (Lond.)*, **136**, 1.
Ladefoged, P., Draper, M. H., and Whitteridge, D. (1958). *Misc. Phonet. (Lond.)*, **3**, 1.
Luchsinger, R. (1953). *Folia phoniat. (Basel)*, **5**, 58.
Opie, L. H., Spalding, J. M. K., and Stott, F. D. (1959). *Lancet*, **1**, 545.
Roos, J. (1936). *Arch. néer. Phon. exp.*, **12**, 1.
Stetson, R. H. (1951). *Motor Phonetics*, 2nd ed. North Holland Pub. Co., Amsterdam.

MATERNAL HEALTH AND MONGOLISM

BY

ALEC COPPEN, M.D., D.P.M.
Institute of Psychiatry, Maudsley Hospital, London

AND

VALERIE COWIE, M.D., D.P.M.
Assistant Director, Medical Research Council, Psychiatric Genetics Research Unit, Maudsley Hospital, London

The genetical basis of mongolism has been established by the recent discovery of an extra chromosome in the cells of affected individuals. The cause of this abnormality, however, remains unknown, but there are reports of associated effects, often connected with maternal status, which may be of aetiological significance.

For this reason much attention has been paid to maternal health and, in particular, to endocrinological, gynaecological, and obstetric abnormalities. With respect to endocrinological changes, early reports were for the most part contradictory and were not supported by objective findings. Thus Dollinger (1921), Myers (1938), and Benda (1949) had reported a high incidence of thyroid abnormalities in the mothers of mongols, but this was not confirmed by Øster (1953).

No objective findings were reported until Ek (1959) and Ek and Jensen (1959) published the results of their investigations into thyroid and adrenocortical function in the mothers of mongols. Ek investigated 41 mothers of mongols and reported that their serum protein-bound iodine (P.B.I.) was significantly raised (mean value 7.1 μg./100 ml.) compared with that of a control group (mean value 5.9 μg./100 ml.). Ek and Jensen also studied the corticoid output in the urine of 20 of these mothers, and found that, though the 17-ketosteroids and 17-ketogenic steroids were normal, certain fractions containing dehydroepiandrosterone and an ether-extractable tetrazolium-salt-reducing ketocorticoid were double the value found in a control group.

Ek also reported that 20 of the 41 patients had marked psychoneurotic symptoms and that the increase in P.B.I. was most marked in these women. This is in keeping with observations of Benda (1949) and Øster (1953, 1956) that there is an increased incidence of nervousness and neurosis in the mothers of mongols.

The present study was designed primarily to investigate further these factors, which may be of possible aetiological significance in mongolism.

The Investigation

The present series consists of 55 mothers of mongols. Their ages ranged from 28 to 61, with a mean of 44.1 years. The mean number of years between the birth of the mongol and the interview in the present investigation was 10.6 years. In each case every effort was made to obtain accurate information from the mother regarding past events, but it was fully realized that distortion of memory occurs with the passage of time, and this is especially so in connexion with the circumstances surrounding the birth of a defective child. None of the mothers had any family history of consanguinity among their forebears. All had borne only one mongol, except one who had borne two mongol daughters.

Medical, gynaecological, and obstetric histories were taken from each mother. A clinical examination was then carried out in each case, special attention being paid to evidence of thyroid dysfunction. In addition, anthropometric measurements were made, the serum P.B.I. was estimated, and a personality questionary was undertaken.

Assessment of Thyroid Function

No clinical evidence of past history of thyrotoxicosis was found in any of the subjects.

The serum P.B.I. is the nearest approach to an estimation of the circulating thyroid hormone at present available. This estimation was carried out in 54 cases. One mother refused to have a venepuncture.

The P.B.I. was estimated according to the method of Grossmann and Grossman (1955). None of the subjects had at the time been taking any drug known to affect the level of P.B.I., and none had had an *x*-ray examination during the previous year. The normal range of values for P.B.I. according to various techniques used is 3–8 μg./100 ml. From a control series of 30 mothers who had not borne mongol children blood was obtained for the estimation of P.B.I. The mean age of this control group was 39.9 years.

TABLE I.—*Protein-bound Iodine*

	Mothers of Mongols (n=54)		Controls (n=39)		Comparison Between Groups	
	Mean	S.D.	Mean	S.D.	t	P
P.B.I. (μg./100 ml.)	4·7	1·0	4·8	0·7	0·7	Not significant
Age (years) ..	45·6	6·6	39·9	10·8	1·92	,,

The group of mothers of mongols did not differ from the control group with respect to the P.B.I. (Table I). Only one of the former group had an abnormally high P.B.I.—8.9 μg./100 ml. There was no thyroid enlargement in her case or any clinical sign of thyroid dysfunction. One mother with a very low normal P.B.I. level of 3.2 μg./100 ml. had a sister who had been diagnosed as a cretin.

Moderate enlargement of the thyroid was found in 9 of the 55 subjects. Ek (1959) found thyroid enlargement in 12 of his series of 41 mothers of mongols.

Psychological Factors

A psychiatric history was taken from each of the mothers, and the incidence of any nervous or mental illness requiring treatment at home or in hospital was noted.

The Maudsley Personality Inventory was applied to each of the mothers. This is a questionary of 48 items devised by Eysenck to measure two personality factors —extraversion and neuroticism. Extraversion refers to the outgoing sociable qualities of the personality. Neuroticism is defined as the general emotional lability of a person and his liability to neurotic breakdown under stress. Neurotic groups of patients have been shown to score consistently higher on the neurotic rating of the inventory (Eysenck, 1959).

None of the subjects in the present series had a history of psychiatric illness. Two had been admitted to hospital for a reactive depression after the birth of the mongol. In each case the shock of having borne a mongol child, coupled with associated stress factors in the environment, was considered by psychiatrists at the time of the breakdown to have been the immediate cause of the depressive illness.

Seven subjects had suffered from mild neurotic symptoms for which they had been treated at home by their general practitioners.

Scores obtained on the Maudsley Personality Inventory (Table II) for both neuroticism and extraversion did not differ significantly from those

TABLE II.—*Maudsley Personality Inventory*

	No. of Subjects	Neuroticism Score		Extraversion Score	
		Mean	S.D.	Mean	S.D.
Mothers of mongols	55	20·8	9·5	26·8	6·1
Controls (present series)	31	20·2	10·2	23·8	8·9
Controls (Eysenck, 1959)	1,800	19·9	11·0	24·9	9·7

Comparison between controls (present series) and mothers of mongols: neuroticism: t=0·273 (not significant); extraversion: t=1·82 (not significant).

obtained from the control group and were in accordance with those obtained by Eysenck (1959) for normal subjects. The results are in agreement with the clinical impression that these subjects showed no marked psychiatric disturbance or personality deviation. Seven of them reported that they had suffered from anxiety during their pregnancy with the mongol. Of these, five were living in environmental circumstances likely to provoke anxiety in the most stable of temperaments.

Physique

The discriminant androgyny score (Tanner, 1951, 1955) was obtained for each patient by measuring the biacromial and bi-iliac diameters and applying the following formula:

$$3 \times \text{biacromial diameter (cm.)} - 1 \times \text{bi-iliac diameter (cm.)}$$

All measurements were made by the same observer, using a Martin anthropometer.

The term androgyny may be defined as the presence of masculine features in women and feminine features in men. Each sex has a characteristic score (90.1 with S.D. 4.7 for men; 78.9. with S.D. 4.6 for women), and only 12% of a normal population of men and women were misclassified by this score (Tanner, 1951). This feature of physique arises at puberty, probably under the influence of the sex hormones, and recent investigations suggest that the androgyny score is associated with other sexual characteristics and abnormalities. Thus Ferriman *et al.* (1957) found that women with hirsuties had an increased urinary 17-ketosteroid output, a tendency to oligomenorrhoea, and an increased biacromial diameter. Raboch (1957) found small biacromial diameters in hypogonadal men with female sex chromatin. Coppen (1958) reported that patients with pre-eclamptic toxaemia have considerably more masculine scores than a control group of normal pregnant women. Thus it is possible that women with a constitutional predisposition to endocrine overactivity, as has been postulated in the case of mothers of mongols, would show abnormalities in their androgyny score. The control group of Coppen (1958), which was practically identical with that of Tanner (1951), was used in the present study.

Height, biacromial and bi-iliac diameters, together with the androgyny scores, are shown in Table III. The

subjects of the present series did not differ significantly from the normal controls (Coppen, 1958) with respect to any of these values.

TABLE III.—*Physique*

	Mongol Mothers (n=55)		Controls (n=50)		Comparison Between Groups	
	Mean	S.D.	Mean	S.D.	t	P
Height (cm.) ..	160·8	5·7	160·0	4·8	0·98	N.S.
Biacromial diameter (cm.)	36·3	1·3	35·9	1·2	1·78	,,
Bi-iliac diameter (cm.)	29·4	1·7	28·9	1·6	1·52	,,
Androgyny score ..	79·7	3·7	78·9	3·3	1·12	,,

A suggestion has been made by Penrose (1951, 1954) that mothers who have borne mongols at a relatively early maternal age may include individuals of specific genetical constitution who may lack the protection afforded by younger maternal age against the conception of a mongol child.

With this in mind, the entire group of mothers in the present series was divided according to age at the mongol birth. The division was made at a point one standard deviation below the mean—that is, at 27 years of age. It was found (Table IV) that the younger group

TABLE IV.—*Maternal Age at Birth of Mongol and Physique*

	Mothers Over 27 (n=38)		Mothers Under 27 (n=16)			
	Mean	S.D.	Mean	S.D.	t	P
Androgyny score ..	78·9	3·8	81·4	3·0	2·32	0·05
Biacromial diameter (cm.)	36·1	1·3	36·9	1·3	2·05	0·05
Bi-iliac diameter (cm.)	29·3	1·6	29·4	1·8	0·03	N.S.

had a significantly higher mean androgyny score and mean biacromial diameter than did the older group. Other measurements made during the investigation, including the P.B.I., however, showed no significant differences between the groups.

A further trend appeared which suggested a possible association between the number of miscarriages and the androgyny score, though the numbers are two small for statistical evaluation. This is shown in Table V. The

TABLE V.—*Mean Androgyny Score and Number of Miscarriages*

Group	No. in Group	Mean Androgyny Score
Mothers with no miscarriages ..	29	79·2
,, ,, one miscarriage ..	15	78·9
,, ,, two miscarriages ..	7	79·9
,, ,, three or more miscarriages	3	83·5

mean androgyny score was found to be raised in groups of mothers who had had two or more miscarriages, but this effect was not seen in groups of mothers who had had one or no miscarriage.

Medical History of the Mother

Øster (1953), in his extensive survey of mongolism in Denmark, observed that illnesses in the mother, with the exception of abdominal tumours, showed a marked tendency to accumulate around the time of birth of the mongol. This has not been observed in the present small series.

Of the mothers with illnesses occurring in the year preceding the mongol's birth, one had a threatened mastoid, one had a perineal abscess, and two had miscarriages. One mother suffered from arterial hypertension, but this had been a constant finding for years before and after the birth of her mongol child. Another mother suffered from mitral stenosis as a sequel to rheumatic fever in childhood.

Of mothers with physical complaints immediately after the birth of the mongol, one had a severe perineal rash, another had an outbreak of carbuncles in various parts of the body, a third suffered from epigastric pain and suspected but unconfirmed peptic ulceration, and a fourth had an operation for displacement of the uterus.

Menstrual and Obstetric History of the Mother

All of the 55 subjects were able to give their age at menarche. The mean age of the series is 14.4, based on the completed year of age, ignoring fractions, with a range of 10 to 19 years.

Øster (1953) found a mean age of menarche of 413 mongol mothers in his series to be 14.48 years, based on the completed year of age, which he found slightly younger than average ages of menarche in Danish urban and rural control groups.

Only two mothers had suffered from irregularity of periods throughout their menstrual histories. A third mother gave the history of one month's amenorrheoa at the age of 26, prior to her miscarriage, when she became obese but had no other complaints. She did not seek medical advice, and the obesity disappeared on a slimming diet. Another, who had a regular but three-weekly menstrual cycle, described greatly diminished menstrual flow for three periods immediately before the conception of the mongol at the age of 39. The effect was so marked that she believed she was menopausal, but after the birth of the mongol she reverted to her normal menstrual pattern, which has continued unchanged, she now being 43 years of age.

The remainder of the subjects gave histories of a regular menstrual cycle of constant duration and amount of flow, up to the onset of the menopause where this had been reached.

Twenty-four mothers had become menopausal by the time of the investigation, taking the time of menopause to be the time when menstrual periods previously regular became irregular. The mean age at the menopause was 47.6, with a range of 36 to 55 years. Øster (1953) found the mother's age at menopause to be remarkably high, in 50% of his cases it not having occurred until after the age of 50. In the present series the mean length of time that had elapsed between the birth of the mongol and the first signs of the menopause was 10.6 years, with a range of 6 months to 19 years. Only two mothers in the series were menopausal at the time of the birth of the mongol. One had been having hot flushes for a year before the conception of the mongol, her periods being regular until that date, but she had no further periods after the birth of the mongol; another had no menopausal signs before the conception of the mongol, but had no further menstruation after the period that terminated the flow of lochia after the mongol's birth. The mother who became menopausal six months after the birth of her mongol child was only 36 when her periods finally stopped.

The mean maternal age at the time of birth of the mongol was 33.5 years, based on the completed year of age, ignoring fractions (range of 22 to 44 years). This figure is comparable to that reported by Øster (1956),

who in 518 mothers found a mean maternal age of 35.1 years at the time of the birth of the mongol. Penrose (1951) found in a pooled sample of 1,038 mongols from widely different sources that the maternal age was 36.6 years (S.D. 7.1). He compared this with the mean maternal age for all births in England and Wales in 1939, which was 28.6 years (S.D. 6.0). The mean ordinal position of the mongol in the conception order was 0.74 ($= \Sigma \frac{m-1}{n-1} / N$, according to Slater, 1958), with a standard deviation of 0.38 and a standard error of mean of 0.05. This indicates that the mongol tends to appear late in the conception order, the expected mean ordinal position being 0.50.

Forty-five of the mothers had already been pregnant prior to the pregnancy with the mongol. Of these, 15 had had miscarriages or stillbirths in the pregnancy immediately preceding that with the mongol. The mean time between the conception of the mongol and the immediately preceding miscarriage or stillbirth was 45.9 months (range, 11 to 196 months). The mean time between the conception of the mongol and the immediately preceding live birth was 48.3 months (range, 13–171 months).

Of the total number of conceptions, 93 in all, prior to the conceptions of the mongols, 28 pregnancies (of which one was counted twice, having preceded the birth of two mongols), or 31%, had ended in abortion or stillbirth. Four of these had been artificially procured.

This figure of 31% is nearly double that obtained by Ingalls *et al.* (1957), who found that of total pregnancies prior to the birth of the mongols the 52 mothers in their series had had 15.5% of such mishaps in past pregnancies, which was much greater than the incidence of 9.4% in their control group. It greatly exceeds that of Øster (1953), who reported 148 stillbirths and abortions, or 9.7%, in 1,523 pregnancies prior to that of the mongol in a series of 515 mothers. The miscarriage rate in the present series is extremely high compared with that estimated by the Biological and Medical Committee of the Royal Commission on Population (1950), who considered that the incidence of spontaneous abortion in the general population lay between 7 and 11% of all pregnancies, and that perhaps 2 to 5% of pregnancies were terminated by induced abortion.

Ingalls *et al.* (1957) has drawn attention to the incidence of vaginal bleeding or spotting in the first three months of pregnancy with a mongol child. In their series about 10% of mothers gave a history of such haemorrhage, and the effect was seen more often in the older mothers of the series. Øster (1953) reports 25 cases of vaginal bleeding or spotting in the first three months of pregnancy with a mongol child, out of 429 cases, or about 5.8%. In the present series, in 9 of the 56 mongol pregnancies, or in 16.1%, the mothers had vaginal bleeding within the first three months. Of these mothers, four were 25 years or under and three were 40 years or older.

Other incidents during the pregnancies with the mongols which were noted were psychological trauma or marked anxiety in nine cases; raised blood-pressure and/or marked swelling of the ankles in eight cases; severe or prolonged periods of vomiting in five cases; and infection of the urinary tract requiring medical treatment in two cases, at nine weeks and eight months respectively.

Discussion

The mean P.B.I. level of the present series of mothers of mongols was 4.8μg./100 ml., which was almost identical with that of the control group, and is well within the limits of normal for the method of estimation used. Thus the present findings differ greatly from those of Ek (1959), who found a mean value of 7.1 μg./100 ml. for the P.B.I. level in his series of 41 mothers of mongols. Moreover, no fewer than 12 subjects in Ek's series had P.B.I. levels of 7.9μ./100 ml. or over.

Ek (1959) reported that no fewer than 20 out of his 41 subjects complained of neurotic symptoms. It was this group that had the higher P.B.I. levels in his series, with a mean of 7.8 μg./100 ml. as compared with a mean of 6.4 μg./100 ml. for the remainder of his subjects, who were classified as less neurotic. Øster (1956) was also impressed by the excess of cases of nervous illness among the relatives of mongols, and that this effect was especially pronounced among the mothers. In the present series, however, there was no evidence of an excessive incidence of neurosis when this is based on the criterion of the necessity for treatment at home or in hospital, and the scores obtained on the Maudsley Personality Inventory were not compatible with increased neuroticism in the group of mongol mothers.

The constitutional difference, as shown by differences in body-build between the younger and older groups of mothers in the present series, is compatible with the view expressed by Penrose (1951, 1954) that some mothers are especially likely to have mongol children by virtue of their genetical constitution. Penrose suggests that their increased susceptibility might be due to a partial suspension of the protective effect of young maternal age.

The main findings in the present series all seem to suggest that an endocrinological imbalance may be commonly present in the mothers of mongols, and the younger group of mothers have a body-build suggestive of constitutional endocrinological imbalance. The high miscarriage rate for the group of mothers as a whole may also be related to endocrinological factors which in the older mothers may be connected with the normal process of ageing and the approach of the menopause.

As the androgyny score and the biacromial diameter appear to be most influenced by the sex hormones and in particular by the androgens, it would be most interesting to have confirmation of the findings by Ek and Jensen (1959) of increased dehydroepiandrosterone output in the mothers of mongols.

A striking finding was the very high rate of miscarriages and stillbirths prior to the birth of the mongol. Attention has been focused on the pregnancies prior to the birth of the affected child, as these are clearly of greater biological significance than those after the mongol, which may have been intentionally restricted by the parents. This seems to indicate that at the time of the conception of the mongol the mother was already susceptible to increased obstetric risks. The connexion between this and the production of a mongol child is not clear, and the relationship may be an indirect one involving perhaps several factors, including increased maternal age and possibly related degenerative changes in the reproductive system of the mother. In view of the most recent finding of chromosomal variation in mongolism, it seems not unreasonable to consider also the possibility of mutation in the germ cells

of the mother leading to the production of a non-viable foetus. Such an idea would be supported if it were found that the miscarriages and stillbirths prior to the pregnancy with the mongol tended to accumulate close to this event. With this in mind, the present material was examined to find whether or not there were an unexpectedly large number of conceptions ending in miscarriage in the conception order immediately prior to the mongol. The results are shown in Tables VI and VII. The difference between the observation of 15 and the expectation of 12.72 is clearly not significant.

TABLE VI.—*Positions of Normal Births and Miscarriages in Relation to Mongol in Conception Order*

Position of Conception in Relation to Mongol	No. of Normal Births	No. of Miscarriages
−5	2	1
−4	5	1
−3	8	5
−2	22	7
−1	29	15
+1	18	2
+2	9	1
+3	1	4
+4	0	3
+5	1	1
+6	0	1
+7	1	0
	96	41

N.B.—One miscarriage was counted twice owing to two mongols occurring in one sibship.

TABLE VII.—*Incidence of Miscarriage Immediately Prior to Mongol in Conception Order*

Conception Order of Mongol	Observed Incidence of Miscarriage in Immediately Preceding Conception	Expected
2	5	3·49
3	4	4·57
4	2	1·83
5	2	0·83
6	2	2·00
Total ..	15	12·72

$$\chi^2=\frac{(2\cdot28)^2}{12\cdot72}=0\cdot41.\quad \text{D.F. 1.}\quad P=0\cdot5.$$

Moreover, when all other possible relationships between the conception order of a miscarriage and the conception of a mongol are considered (see Table VII), it is found that no single relationship is favoured at the expense of others: thus there is approximately the same expectation of a miscarriage before as after the birth of a mongol.

Summary

Fifty-five mothers of mongols were examined. The findings failed to confirm earlier reports of thyroid abnormality, including raised serum P.B.I. The body-build of the group as a whole did not differ from normal. When the group, however, was examined according to maternal age at the time of the mongol birth, it was found that the group of mothers bearing a mongol at 27 years of age or younger had a significantly raised mean androgyny score and mean biacromial diameter. A tendency was also observed for the mothers with multiple miscarriages to have a raised androgyny score. Psychological testing and general medical history failed to show deviations from normal. The obstetric histories, however, showed an extremely high rate of miscarriage irrespective of conception order and unrelated to birth order of the mongol.

We are grateful to Dr. D. R. C. Willcox, consultant pathologist, Bethlem Royal and Maudsley Hospitals, for his help and advice in this work, and to his department for the estimation of the P.B.I. We thank Professor L. S. Penrose for his helpful advice and criticism. We are also grateful to Dr. L. T. Hilliard and Dr. B. H. Kirman for their kindness in allowing us to examine the mothers of patients at the Fountain Hospital, and to Miss Dickinson and Miss Burgess, of the Fountain Hospital, for their invaluable assistance in arranging the appointments.

REFERENCES

Benda, C. E. (1949). *J. Amer. med. Ass.*, **139**, 979.
Coppen, A. J. (1958). *J. psychosom. Res.*, **2**, 241.
Dollinger, A. (1921). *Z. Kinderheilk.*, **27**, 332.
Ek, J. I. (1959). *Acta paediat. (Uppsala)*, **48**, 33.
—— and Jensen, C. C. (1959). *Acta endocr. (Kbh.)*, **31**, 523.
Eysenck, H. J. (1959). *The Manual of the Maudsley Personality Interview*. London.
Ferriman, D., Thomas, P. K., and Purdie, A. W. (1957). *Brit. med. J.*, **2**, 1410.
Grossmann, A., and Grossmann, G. F. (1955). *J. clin. Endocr.*, **15**, 354.
Ingalls, T. H., Babbott, J., and Philbrook, R. (1957). *Amer. J. Obstet. Gynec.*, **74**, 572.
Myers, C. R. (1938). *Proc. Amer. Ass. ment. Defic.*, **62**, 142.
Øster, J. (1953). *Mongolism*. Danish Science Press, Copenhagen.
—— (1956). *Dan. med. Bull.*, **3**, 158.
Penrose, L. S. (1951). *J. ment. Sci.*, **97**, 738.
—— (1954). *Lancet*, **2**, 505.
Raboch, J. (1957). *J. clin. Endocr.*, **17**, 1429.
Royal Commission on Population (1950). Papers, Vol. 4: Reports of the Biological and Medical Committee. H.M.S.O., London.
Slater, E. (1958). In *Symposium on Nuclear Sex*, edited by D. R. Smith and W. M. Davidson. Heinemann, London.
Tanner, J. M. (1951). *Lancet*, **1**, 574.
—— (1955). *Growth at Adolescence*. Blackwell, Oxford.

INFLUENZAL ENCEPHALOPATHY AND POST-INFLUENZAL ENCEPHALITIS

HISTOLOGICAL AND OTHER OBSERVATIONS

BY

J. G. HOULT, M.B., D.C.H., D.Path.

AND

T. H. FLEWETT, M.D.

Dudley Road Hospital, Birmingham, the Midland Centre for Neurosurgery, Smethwick, and the Regional Virus Laboratory, Little Bromwich Hospital, Birmingham

Cases of neurological disorder associated with influenza have been reported for many years; perhaps it is merely because laboratory investigation has become so much more widely available that more cases have been reported associated with Asian influenza than with previous epidemics or pandemics. We (Flewett and Hoult, 1958) reported 12 such cases. Six of these presented neurological symptoms after the acute attack of clinical influenza had subsided, and all but one recovered; the others were cases of clinical "encephalitis" with convulsions or "fits" proceeding to coma and death, which occurred during the acute phase of an attack of influenza, and which showed a very congested brain at necropsy; we found no obvious histological lesions in a few sections of paraffin-embedded material. This paper describes the results of detailed histological examinations of the brains of five of these patients. The first were children, aged between 5 and 13, who died at intervals of seven to nine days after the onset. The fifth patient was a man aged 44 who died 11 days after the onset.

Methods

Large blocks were taken from the following sites and embedded in celloidin: spinal cord (in some cases only),

medulla, pons, mid-brain, basal ganglia, frontal, occipital, parietal, and temporal lobes, and cerebellum. Sections were stained with cresyl violet, Woelcke's method for myelin, phosphotungstic acid–haematoxylin, and van Gieson. Some sections were also stained with luxol-fast blue and counterstained with cresyl violet.

A virus was isolated or the complement-fixation test on the post-mortem blood was positive in four patients.

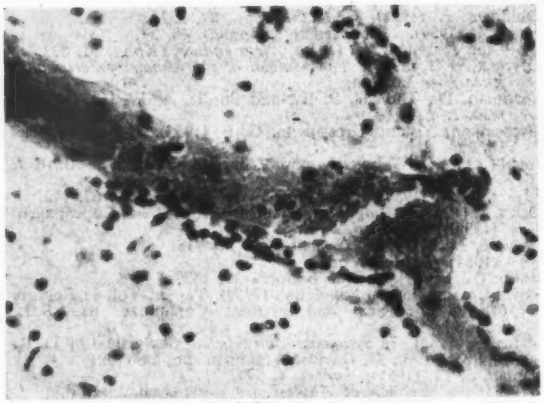


FIG. 1.—Slight perivascular infiltration by lymphocytes. (Cresyl violet. ×90.)

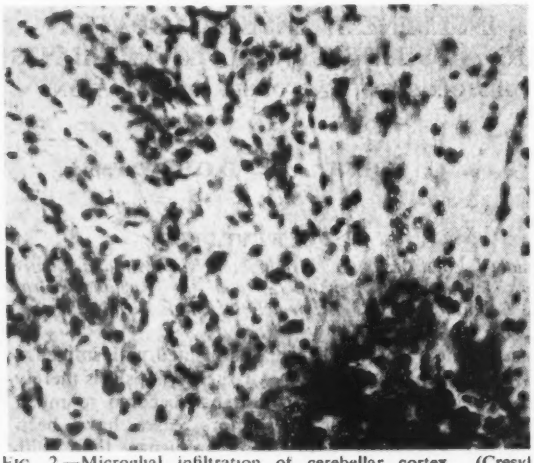


FIG. 2.—Microglial infiltration of cerebellar cortex. (Cresyl violet. ×375.)

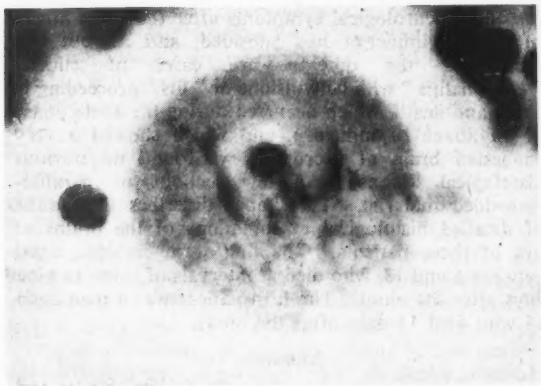


FIG. 3.—Body of a Purkinje cell, showing folding of nuclear membrane. (Cresyl violet. ×1,600.)

No serum was taken or virus isolated from the last case, but the clinical history supported a diagnosis of influenza, and the lung histology was consistent with the history of influenza of 11 days' duration.

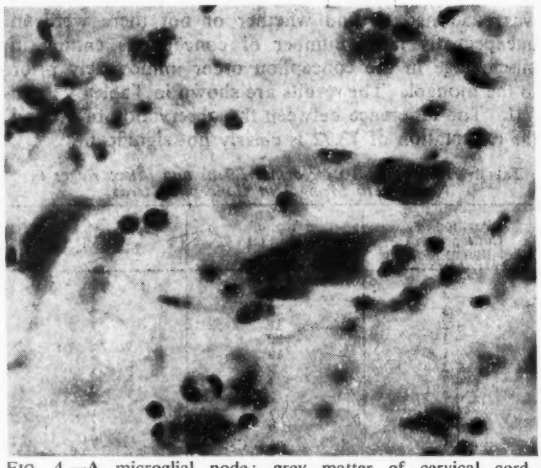


FIG. 4.—A microglial node; grey matter of cervical cord. (Cresyl violet. ×500.)

FIG. 5.—Cerebellar cortex, showing severe loss of cells in the granular layer. (Cresyl violet. ×75.)

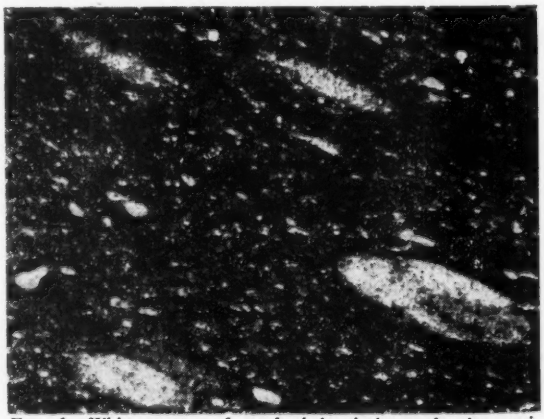


FIG. 6.—White matter of cerebral hemisphere, showing perivascular demyelination. (Woelcke's stain. ×45.)

Results

No gross histological abnormalities were found in the brain except in Case 5. Such changes as were found had to be patiently sought over many sections, and might well have been missed in the small routine paraffin sections. The changes found consisted in: (1) Scanty and patchy lymphocytic infiltration of meninges and perivascular spaces. These were found chiefly over, in, and just beneath occipital, temporal, and cerebral cortex, except in one case in which no histological abnormality could be found at all (Cases 1, 2, 3, and 5) (Fig. 1). (2) Microglial proliferation and formation of microglial nodes in the cerebellar cortex, together with patchy loss of Purkinje cells; some of these cells also showed a folding of the nuclear membrane (Figs. 2, 3, and 4). The distribution of the microglial lesion in Fig. 2 suggests a reaction to the death of a Purkinje cell. Several such lesions were found in the cerebellum of this patient; but no cells were found in an early stage of degeneration such as might throw light on its cause.

It is of interest that Fraser *et al.* (1959) observed, by marking infected cells with fluorescent antibody, that Purkinje cells of both infant and adult mice were infected by neurotropic strains of influenza virus, and in infant mice could be infected with non-neurotropic virus also. The lesion in Fig. 4 also suggests a reaction to the destruction of a neurone in the spinal cord; the adjacent neurone has lost its Nissl substance. Another case showed a more extensive lesion in which many of the dwarf neurones of the granular layer appeared to have undergone autolysis without giving rise to any obvious inflammatory reaction (Fig. 5).

The fifth case resembled histologically that described by Henson and Russell (1942) and Russell (1955) as acute haemorrhagic leuco-encephalitis. The lesions appeared to be of recent origin in that there was some infiltration with microglia and an occasional polymorph; but new gliofibrils had not been laid down around the affected blood-vessels, and the erythrocytes in the "ring haemorrhages" still showed normal morphology and staining reaction. The lesions were widely distributed in the white matter of the cerebral hemispheres; not all showed gross haemorrhage, though a few erythrocytes could almost always be found in the zone of perivascular damage; the zone of demyelination did not extend far from the vessels (Fig. 6: lesions with little haemorrhage were selected for illustration to show the extent of demyelination).

With the exception of the last case, the cellular lesions, irregularly distributed as they were, might perhaps be explained as the consequences of small infarcts due to emboli from pneumonic lungs; and the scanty round-cell infiltration of the pia-arachnoid and the perivascular spaces might be a reflection of small lesions of this kind in the neighbouring brain substance; it seems unnecessary to postulate intracerebral multiplication of virus or any specific toxic effect of the virus, though of course this could not be excluded.

Discussion

All the cases we have described here, with the exception of the fifth case, were mentioned in our last paper. It so happened that only two patients showing a picture of perivascular demyelination and in whom a firm diagnosis of epidemic influenza could be made came to necropsy—the last case described above and the one previously described that presented with acute ascending paralysis. It is quite likely that the cases described by us that developed encephalitic symptoms with abnormal cerebrospinal fluids some days after recovering from influenza may have had lesions of this type. They recovered, so histological evidence is not available. Presumably the fatal cases encountered by McGill and Goodbody (1958) and Goodbody and McGill (1958) were all of this type. Post-influenzal encephalitis is so rare that probably no one pathologist will see enough cases to find all the varieties of histological picture described by others.

Furthermore, because this form of encephalitis is so rare, it is almost impossible to be sure that its association with influenza is significant; cases of encephalitis do occur from time to time, and may be expected to continue to occur during any epidemic. However, Kapila *et al.* (1958), describing a number of cases of neurological disorder associated with influenza in India, estimated that the normal incidence of encephalitis in two stations from which patients were admitted was two or three cases a year, whereas during the influenza epidemic 21 cases occurred within a month; we know of no other series in which such a comparison has been made. Furthermore, Kapila *et al.* were able in four of their cases to exclude by serological means infection by arthropod-borne viruses of groups A and B. Their paper thus affords the best evidence so far that the association is not a chance one.

When the symptoms come on some days after the acute attack of influenza, it is probably not valid to make a distinction between the encephalitic variety (shown by Case 5, described above) and the spinal variety, resembling clinically the Guillain–Barré syndrome (as shown in Case 4, described in our last paper), since the lesions were essentially of the same nature—namely, perivascular demyelination—though the distribution in the central nervous system was different. The nosological identity of such conditions has been supported by Russell (1955). If this identity be accepted, then from our experience it appears that there are two principal forms of major neurological disturbance associated with influenza: (1) an acute encephalopathic variety, with minimal histological lesions, occurring early in the attack of influenza, and (2) the perivascular demyelinating leuco-encephalitis of the type described as a post-infective sequel to a number of other acute virus infections—measles, varicella, etc.

A third type of encephalomyelitis, closely resembling acute paralytic poliomyelitis, both clinically and histologically, was associated with the Asian influenza pandemic in Italy (Battaglia *et al.*, 1959), but these authors do not mention any attempt to exclude infection with polio virus.

It is tempting to speculate, in accordance with modern immunological concepts, that damage occurs in the acute phase, whether by a toxin or by actual virus multiplication, that products of such damage are liberated into the blood, giving rise to anti-brain antibodies, and that these, becoming fixed in brain substance around blood-vessels, somehow cause disintegration of the myelin. This may be so; but there is, unfortunately, no evidence to support it, other than the demonstration that similar lesions can be provoked in guinea-pigs or rabbits, and occasionally in man, by injecting suspensions or extracts of nervous tissue.

Summary

Histological examination of brains of four children and one man dying with encephalitic symptoms within a few days of an attack of Asian influenza showed, in the children, scanty microglial infiltrations principally in the cerebellar cortex and also in the spinal cord; in the man, an acute haemorrhagic leuco-encephalitis. In one brain no abnormality other than congestion could be found. The remainder showed also slight lymphocytic infiltration of the perivascular spaces and meninges.

We are indebted to those physicians named in our last paper who allowed us to report their cases and supplied us with clinical details; to Professor Stuart-Harris for reading our draft, and especially to Dr. A. L. Woolf for his helpful comments and criticisms, and for drawing our attention to the nuclear changes in the Purkinje cells.

REFERENCES

Battaglia, S., Guazzi, G. C., Macchi, G., and Masini, T. (1959). *Acta neurol. belg.*, **59**, 123.
Flewett, T. H., and Hoult, J. G. (1958). *Lancet*, **2**, 11.
Fraser, K. B., Nairn, R. C., McEntegart, M. G., and Chadwick, C. S. (1959). *J. Path. Bact.*, **78**, 423.
Goodbody, R. A., and McGill, R. J. (1958). *Brit. med. J.*, **2**, 1294.
Henson, R. A., and Russell, D. S. (1942). *J. Path. Bact.*, **54**, 227.
Kapila, C. C., Kaul, S., Kapur, S. C., Kalayanam, T. S., and Banerjee, D. (1958). *Brit. med. J.*, **2**, 1311.
McGill, R. J., and Goodbody, R. A. (1958). *Lancet*, **1**, 320.
Russell, D. S. (1955). *Brain*, **78**, 369.

MUMPS MENINGO-ENCEPHALITIS

BY

H. G. S. MURRAY, M.B., B.Ch.
Assistant Lecturer, Department of Microbiology, the Queen's University of Belfast

C. M. B. FIELD, M.D., M.R.C.P.Ed.
Consultant Paediatrician, the City Hospital, Belfast

AND

W. J. McLEOD, M.D., D.P.H.
Senior Medical Officer, Belfast Health Department

During 1958 there was an epidemic of mumps in Northern Ireland which was associated with an increased prevalence of mumps meningo-encephalitis. It is the purpose of this paper to present the clinical, laboratory, and epidemiological finding in 50 cases of mumps meningo-encephalitis. Five occurred in 1957, 39 in 1958, and six in 1959.

Laboratory Diagnosis

Where possible, two samples of serum from each patient were obtained for determination of complement fixation antibody titres. The first, "acute," serum was taken as soon as possible after the onset of illness. The second, "convalescent," serum was usually taken about three weeks after onset. These are together referred to as "paired sera." V and S mumps antigens (see Kravis, Sigel and Henle, 1951), 2½ MCD_{50} of complement, and overnight fixation were used in the tests. The diagnosis in 42 cases was based on the demonstration of a fourfold or greater rise in complement fixation antibody in paired sera. In one case the sera were taken three weeks (anti-V = >1:512; anti-S = 1:64) and five weeks (anti-V = 1:256; anti-S = 1:16) after the onset of mumps, so that the antibody titres were on the wane. Six out of seven cases in which only single samples of serum were tested had clinical salivary-gland involvement. In all but one the anti-V antibody titre was 1:128 or higher. The single exception in which the serum was taken approximately six weeks after onset of parotitis had anti-V and anti-S antibody titres of 1:32 and 1:64 respectively.

Of 40 sera taken within seven days of onset of symptoms of mumps meningo-encephalitis, sixteen had an antibody titre of <1:8 against V and S antigens, and 5 were tested against V antigen only. Of the remaining 19 the anti-V was higher than the anti-S antibody titre in 11 cases, in one case they were equal, and in seven cases the anti-S exceeded the anti-V antibody titre, thus allowing a presumptive diagnosis of mumps virus infection to be made within the first week of illness in these cases (Kravis *et al.*, 1951). Of the 49 serum samples taken after the seventh day of illness which were tested against V and S antigens, four showed an anti-S > anti-V antibody pattern.

Clinical Findings

The age and sex of the patients are summarized in Table I. It will be seen that 84% of the cases occurred in children under 15 years of age and that males were more commonly affected than females in a ratio of more than 2:1.

Twenty-seven of the patients had parotitis and/or other salivary-gland involvement, but in 23 there was no evidence of salivary-gland involvement.

Apart from the presence or absence of parotitis the clinical findings were essentially the same in the two groups, and these are summarized in Table II. The principal features were fever, neck rigidity, vomiting, and headache. Somnolence was present in 14 patients. Two patients were delirious.

One child, a girl of 6½ years, without salivary-gland involvement, developed complete ophthalmoplegia and was subjected to ventriculography. This patient was apyrexial throughout her illness, and the C.S.F. on the third day of illness showed no abnormality. Sera taken on the third and nineteenth days of illness had anti-V and anti-S antibody titres of 1:64 and 1:8, and 1:256 and 1:16 respectively.

A woman aged 26, who aborted after seven weeks' amenorrhoea, developed pyrexia, neck stiffness, vomiting,

TABLE I.—*Age Distribution of Mumps Meningo-encephalitis*

Age	Salivary-gland Involvement				Total
	Present		Absent		
	Male	Female	Male	Female	
0–4	4	1	5	2	12
5–9	17	1	8	2	28
10–14	1	0	1	0	2
15 and over	0	3	0	5	8

TABLE II.—*Frequency of Clinical Features in Patients with Mumps Meningo-encephalitis*

Clinical Features	Salivary-gland Involvement		Clinical Features	Salivary-gland Involvement	
	Yes	No		Yes	No
Fever	24	20	Sore throat	2	2
Neck rigidity	20	18	Vertigo	2	2
Vomiting	20	18	Photophobia	1	3
Headache	19	17	Listlessness	2	1
Somnolence	9	5	Urinary symptoms	1	1
Lucid and alert	6	4	Delirium	2	0
Irritability	6	3	Ataxia	1	0
Abdominal pain	5	3	Dysarthria	1	0
Anorexia	4	4	Paresis	0	1
Constipation	1	5	Upper respiratory symptoms	0	1
Nausea	2	4	Aches and pains	0	1
Eye signs	1	5			

and weakness of the back muscles 24 hours after curettage. She had no parotitis or other swelling of the salivary-glands. The C.S.F. contained 180 leucocytes per c.mm. (49% lymphocytes, 51% polymorphs). Poliomyelitis was suspected but no enteric virus was isolated from the faeces. A serum sample taken on the eighth day of illness was found to have a mumps anti-V antibody titre of 1:64 and anti-S 1:128. Unfortunately a convalescent specimen or serum was not available.

A 6-year-old boy with a three-year history of epilepsy was admitted to hospital with somnolence and ataxia of one week's duration after an attack of mumps three weeks prior to admission. Serum taken on admission showed antibody titres of >1:512 and 1:64 against mumps V and S antigens respectively. Examination showed ataxia, a positive Romberg sign, dysarthria, and nystagmus. The C.S.F. taken 55 days from onset of neurological symptoms contained less than 1 cell per c.mm. and 35 mg. of protein per 100 ml., but an E.E.G. showed deterioration compared with a previous record made one year previously. He was discharged two weeks later after gradual improvement and disappearance of abnormal physical signs. This boy has been readmitted to hospital on two occasions with episodes of vomiting and worsening ataxia and incoordination.

Encephalitis of post-infective type occurred in a boy aged 6 years who developed headache, pyrexia, and neck rigidity three weeks after an attack of mumps. His condition improved and he was free from symptoms within five days. An attempt at lumbar puncture was unsuccessful. On the sixteenth day after the onset of neurological symptoms signs of meningeal irritation reappeared with photophobia, somnolence, and irritability. The C.S.F. was blood-stained but showed no excess of leucocytes; the protein was 240 mg./100 ml., and sugar 72 mg./100 ml. On the nineteenth day of illness he was apyrexial, had mild meningeal signs, and was dull and irritable but well orientated. The C.S.F. contained 64,000 red blood cells per c.mm and 137 white cells (45% polymorphs), protein 242 mg./100 ml., and sugar 74 mg./100 ml. Next day he died, though he appeared brighter, was free from headache, and showed less evidence of meningeal irritation. Serum taken on the twentieth day after onset of neurological symptoms showed anti-V and anti-S antibody titres of 1:32 and 1:64 respectively.

Abdominal symptoms were present in nine patients in the present series.

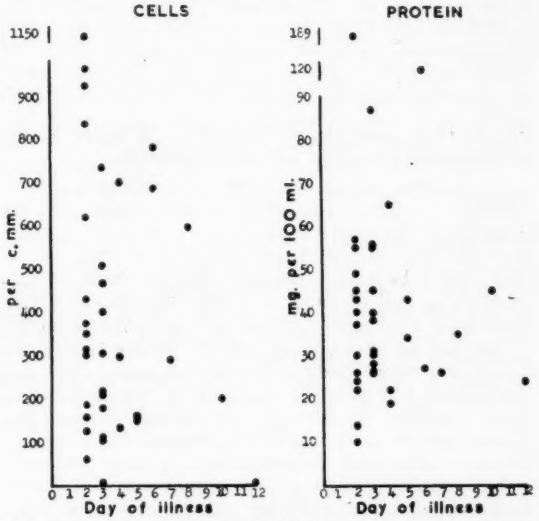
Oophoritis was diagnosed in a girl aged 18 who had marked tenderness in both iliac fossae. Parotitis, with headache, lethargy, and drowsiness, had begun almost one week before abdominal symptoms. This patient had no definite signs of meningeal irritation and the C.S.F. on the twelfth day of illness was normal (5 cells per c.mm.; protein 24 mg./100 ml.). Serum taken 23 days after onset of illness had anti-V and anti-S antibody titres of 1:256 and 1:64 respectively.

Of considerable interest is the case of a girl aged 9, on whom a laparotomy was performed because of abdominal pain, tenderness, and rigidity, in addition to signs of meningeal irritation. Though enlargement of the left parotid and submandibular salivary glands occurred four days after onset of symptoms, specimens of serum taken on the fourth and twenty-second days of illness had on repeated tests complement-fixing antibody titres of <1:4 against V and S antigens. The C.S.F. on the second day of illness showed pleocytosis with 60% lymphocytes and a raised protein content. This case is not included among the 50 in this series, because the clinical diagnosis was not confirmed by serological tests.

Of the 27 patients with salivary-gland involvement parotitis was present in 11 before the symptoms and signs of meningo-encephalitis, and in six patients neurological manifestations preceded enlargement of the salivary glands. Parotitis and neurological features occurred more or less simultaneously in seven patients. In the remaining three it was not possible to establish the sequence.

C.S.F. Examinations

Cerebrospinal fluids from 36 of the patients, obtained during the first 12 days of illness, were suitable for examination. The values for cells and protein are presented in the accompanying Chart.



Cell counts and protein estimations in patients with mumps meningo-encephalitis.

The C.S.F. findings were similar in the patients with parotitis and those without. There was no obvious relationship between the cell counts or protein levels and the day of illness on which lumbar puncture was done. Lymphocytes were the predominant cells in all but two C.S.F. samples in which only about 50% of the cells were lymphocytes.

Usually C.S.F. cell counts were in the hundreds, but in one case 1,150 lymphocytes per c.mm. were found on the second day after the onset of neurological symptoms. This patient had parotitis and an eightfold rise in mumps anti-V and anti-S antibodies in paired sera.

Protein levels in the C.S.F. were in most cases either normal or slightly raised. The highest level found was 189 mg./100 ml. from a case without salivary-gland involvement; paired sera taken on the second and forty-first days of illness showed a diagnostic rise in mumps antibodies (anti-V, 1:32–1:128; anti-S, <1:8–1:8). There were two cases, one of encephalitis and one with oophoritis, in which the C.S.F. findings were normal.

Epidemiology

The monthly incidence of meningo-encephalitis caused by mumps virus in Northern Ireland during 1957–9 is shown in Table III. Unfortunately it is not possible to give any time relationship between the incidence of meningo-encephalitis due to mumps virus and uncomplicated mumps.

In 33 of the homes where a case of meningo-encephalitis had occurred inquiries were made in order to try to find out (*a*) if there was any association between cases of meningo-encephalitis due to mumps virus, (*b*) the order in which parotitis or meningo-encephalitis

TABLE III.—*Monthly Incidence of Mumps Meningo-encephalitis, With and Without Salivary-gland Involvement*

	1957		1958		1959	
	With	Without	With	Without	With	Without
January			2	—	—	—
February			—	1	—	—
March	1	1	1	1	—	2
April	—	—	2	5	—	1
May	1	—	6	1	—	—
June	—	—	4	4	1	—
July	1	—	2	2	1	—
August	—	—	—	2	1	—
September	—	—	1	—		
October	—	—	—	—		
November	—	—	2	3		
December	1	—	—	—		

affected other members of the family, and (*c*) the health of the patient about one year after infection.

In 25 homes there had been no previous cases of mumps or aseptic meningitis in the family and no evidence of the source of infection. In seven families there had been a case of uncomplicated mumps two to three weeks before the patient's illness. In 21 homes in which a case of meningo-encephalitis had occurred there were susceptible siblings—that is, children under 15 years of age who had no previous history of mumps. In 12 of these homes the patient with meningo-encephalitis had parotitis, and further spread occurred in five families. In the other nine homes in which the patient had no salivary-gland involvement there was no spread to susceptible children. One of these "homes" was a residential nursery accommodating 40 children between 2 and 5 years of age. Their contact with the case of meningo-encephalitis was close, yet no other clinical cases of mumps or meningo-encephalitis were observed. These observations suggest a low infectivity in the absence of clinical involvement of the salivary glands.

One young adult and two children aged 5 and 8 years complained of recurrent headaches, and three children were said to be very nervous since their illnesses. One of the latter had been absent from school for three months and was downgraded on his return, but soon regained his normal grade. Physical examination of these patients about one year after infection revealed no abnormalities.

Discussion

Mumps virus can affect many organs, with or without involvement of the salivary glands. The frequency with which the C.N.S. is affected is unknown, and in the absence of notification or of school records of the cause of absenteeism it is not possible to make an estimate. When infection of the C.N.S. occurs it appears to be mainly a meningeal infection, but symptoms of encephalitis with or without meningeal signs were present in about one-third of the cases. Our findings in this respect are very similar to those of Kravis *et al.* (1951). The diagnosis is relatively easy if there is salivary-gland involvement, but when this is absent an accurate diagnosis can be made only by laboratory tests. Mumps meningo-encephalitis was provisionally diagnosed in a number of patients in 1958 because of the prevalence of uncomplicated mumps or because of definite contact with a known case of mumps. This was, however, unusual, and a variety of provisional diagnoses, including aseptic meningitis, non-paralytic poliomyelitis, tuberculous meningitis, and cerebrospinal fever, were made. In the follow-up it was found that the illness was vividly remembered by the parents partly because of its alarming onset and partly because of the serious nature of many of the provisional diagnoses.

The protein and cellular content of the C.S.F., while assisting in the diagnosis, will not necessarily distinguish mumps infection of the C.N.S. from infection with polioviruses, Coxsackie and Echo viruses, Weil's disease, or irritative meningo-encephalitis due to a brain tumour or abscess. In one of the patients in this series ventriculography to exclude a space-occupying lesion might have been avoided if serological tests had first been done. The diagnosis depends on complement-fixation tests, and if viral (V) and soluble (S) antigens are used a presumptive diagnosis may be made in the first week of illness in some cases. Serology is used in preference to attempts at virus isolation because of the irregularity with which the latter can be accomplished.

Complete recovery usually occurs, but 18% of the present series who were followed up were found to be complaining of headache or "nervousness" when seen a year later. In none were any severe sequelae observed. Residual disabilities such as diverse eye and ear symptoms or mental symptoms of a neurasthenic nature both with or without headaches, though relatively uncommon, have been recorded by Oldfelt (1949), Kravis *et al.* (1951), Ritter (1958), and others. Such sequelae, as might be expected, appear to be more common when signs of encephalitis have been present. Nothing is known of the lesions which mumps virus produces in the C.N.S., and there is no evidence that demyelinating lesions occur in mumps infection of the C.N.S. except in the very rare post-infective type of encephalitis. In general it was concluded from our follow-up that a good prognosis can be made in mumps meningo-encephalitis.

Our own observations and those of others, including Enders, Cohen, and Kane (1945), Kilham (1949), and Kravis *et al.* (1951), have shown that mumps meningo-encephalitis is more common in boys than in girls. There is no obvious explanation for this sex difference.

Of the patients with mumps meningo-encephalitis in Northern Ireland, 46% had no salivary-gland involvement. This is remarkably similar to what was observed by Kravis *et al.* (1951) and Ritter (1958), who found no salivary-gland involvement in 49% and 43% of infections respectively Ritter has reported that he found a predominance of meningo-encephalitis *with* parotitis in the spring and of meningo-encephalitis *without* parotitis in the summer. (His conclusion was based on 30 patients over a period of five years.)

Our findings do not support this, as may be seen from Table III, for the peak incidence of mumps meningo-encephalitis cases both with and without parotitis occurred in the late spring and early summer months. But, as already noted, we do not know whether the peak incidence of meningo-encephalitis and of uncomplicated salivary-gland infection coincided. Russell and Donald (1958) described an epidemic of mumps in Gurkha troops in Malaya and noted that all the meningo-encephalitis cases occured in the course of a few weeks towards the latter part of the epidemic. They suggested that the virus might have acquired an increased neurotropism during the epidemic and that separate strains with increased affinity for the C.N.S. might have arisen. Our observations suggest that cases of mumps meningo-encephalitis without parotitis are more or less "dead-end" infections in that patients with meningo-encephalitis *without* parotitis are, as might be expected, less infectious than patients *with* parotitis. We have no

evidence which suggests that patients with meningo-encephalitis give rise to cases of meningo-encephalitis or that meningo-encephalitis cases are caused by a "separate" neurotropic strain. The prevalence of mumps meningo-encephalitis in Northern Ireland in 1958 may have been due to a mumps virus of increased neurotropism, or may simply have been the reflection of a large epidemic of mumps and an available viral diagnostic laboratory whereby infection of the C.N.S. with mumps virus could be differentiated from non-paralytic poliomyelitis and other causes of aseptic meningitis and encephalitis.

Summary

The clinical, laboratory, and epidemiological features of 50 cases of mumps meningo-encephalitis are described. 39 of these occurred during 1958, when there was a mumps epidemic in Northern Ireland. The diagnosis in all cases was confirmed by complement-fixation tests using V (viral) and S (soluble) antigens. The C.S.F. findings in 36 cases are presented. Males were more commonly affected than females, and 84% of the cases occurred in children under 15 years of age.

The principal clinical features were fever, headache, neck rigidity, and vomiting with or without salivary-gland involvement, which occurred in only 54% of the cases. About one-third of the patients showed signs of encephalitis, one of which was of the post-infective type.

The peak incidence of mumps meningo-encephalitis occurred in the late spring and early summer months, and there was no difference in the seasonal incidence of mumps meningo-encephalitis with parotitis and mumps meningo-encephalitis without parotitis. Mumps virus infection appears to have been more readily transmitted by patients with parotitis than by patients without enlarged salivary glands.

A follow-up study of a number of patients was done, and the absence of serious sequelae in this series suggests that a good prognosis may usually be given in mumps meningo-encephalitis.

We wish to acknowledge the co-operation of many clinicians in the preparation of this paper and of the clinical pathologists who provided data on the C.S.F. In particular we would like to thank Drs. F. F. Kane, G. F. W. Tinsdale, and A. R. Crawford, of the Northern Ireland Fever Hospital, and Dr. S. N. Donaldson for their help, and Mr. J. J. McAlister, F.I.M.L.T., and Mr. D. C. Wilson, F.I.M.L.T., for technical assistance in the Virus Reference Laboratory, which is supported by the Northern Ireland Hospitals Authority. We thank Professor G. W. A. Dick for help in the preparation of this paper, and Dr. D. S. Dane for his valuable criticism.

REFERENCES

Enders, J. F., Cohen, S., and Kane, L. W. (1945). *J. exp. Med.*, **81**, 119.
Kilham, L. (1949). *Amer. J. Dis. Child.*, **78**, 324.
Kravis, L. P., Sigel, M. M., and Henle, G. (1951). *Pediatrics*, **8**, 204.
Oldfelt, V. (1949). *Acta med. scand.*, **134**, 405.
Ritter, B. S. (1958). *J. Pediat.*, **52**, 424.
Russell, R. R., and Donald, J. C. (1958). *Brit. med. J.*, **2**, 27.

The Australian Director-General of Medical Services for the Army, Major-General W. D. REFSHAUGE, is to become Australia's Director-General of Health. The present permanent head of the Department of Health, Dr. A. J. METCALFE, will retire later this year. Major-General Refshauge, who is 47, is a graduate of Melbourne University, and is at present engaged in work for the Department of Defence.

SERUM INSULIN IN A CASE OF SEVERE DIABETES MELLITUS SHOWING REMISSION

BY

K. W. TAYLOR,* M.A., Ph.D., M.B., B.Chir.
Department of Biochemistry, University of Cambridge, and Addenbrooke's Hospital, Cambridge

Increasing interest has latterly been shown in cases of severe diabetes showing remission (Goadby, 1943; Harwood, 1957; Phillips, 1957; Peck, Kirtley, and Peck, 1958; Stutman and Hayes, 1959), and some recent correspondence in the *British Medical Journal* has emphasized that clinical remission in the more severe forms of the disease may be commoner than is perhaps realized (Waddell, 1959; Wolff, 1959; Paton, 1959).

Serum insulin studies in a case in which spontaneous remission took place from a state of severe diabetic ketosis are described below. While this case was less severe than some of those reported by the authors above, and even in clinical remission an impairment of glucose tolerance remained, observations on serum insulin and insulin antagonists have not hitherto been reported in this type of patient. In view of current interest in this aspect of diabetes, it seemed worth while to give a detailed account of these studies for the light they may throw on serum insulin in early diabetes.

Case Report

A married professional man, aged 33, attended the out-patient department in May, 1959, with a one-month history of increasing thirst, polyuria, and lassitude, and during this time his weight had decreased from 9 st. 7 lb. to 8 st. 11 lb. (60.3 to 55.8 kg.). Until this period he had been well, without significant earlier illness, nor was there any family history of diabetes. Detailed examination did not reveal any abnormal physical findings, apart from evidence of early dehydration, though his breath smelt strongly of acetone. Intercurrent infection appeared to be absent. The urine then contained over 2% of sugar and gave a strong positive ferric-chloride reaction for acetoacetic acid. The blood-sugar at the time of examination was 352 mg./100 ml. The patient was admitted for stabilization of his diabetes, and after an uneventful period in hospital was discharged on a dose of 20 units of soluble insulin in the morning, 14 units in the evening, and a suitable diet containing 200 g. of carbohydrate.

After severe hypoglycaemia his insulin dosage was reduced to 12 units in the morning and 10 units in the evening and he was instructed to reduce the dosage still further if hypoglycaemia continued. In July, 1959, as a result of increasingly severe hypoglycaemic episodes, he was taken off insulin entirely, and has remained without insulin until the time of writing (January, 1960). During this period he has remained symptom-free, with blood-sugars, taken at an afternoon clinic which he was attending at six-weekly intervals, ranging from 84 to 134 mg./100 ml. His weight has increased to and has remained at 9 st. 4 lb. (59 kg.). An oral glucose-tolerance test, performed in September, 1959, was, however, definitely diabetic in type. Thus, after 50 g. of glucose the blood-sugar rose from a fasting level of 125 mg. to 177 mg./100 ml. at half an hour, and 245 mg. at one hour, falling to 217 mg. at two hours after the glucose. It is clear, therefore, that diabetes in this patient remains quiescent, and that remission is in no sense complete.

Methods

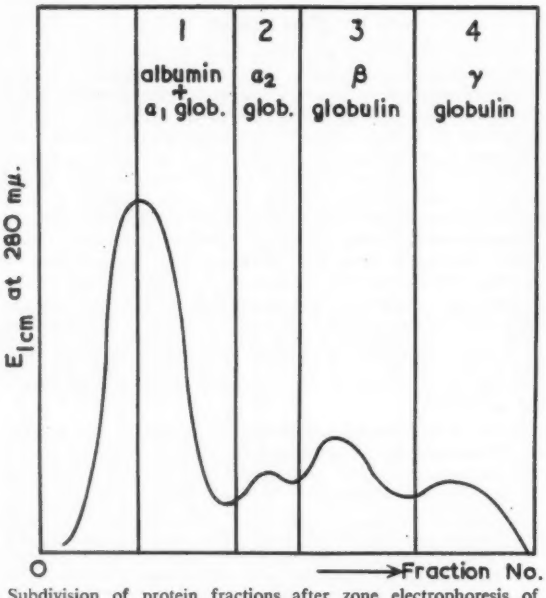
Serum Samples.—Samples of blood were drawn from an antecubital vein into a clean dry syringe. After allowing

*Present address: Baker Clinic Research Laboratory, New England Deaconess Hospital, Boston, Mass.

the blood to clot, the serum was separated from the cells by centrifugation. A sample of blood was obtained for investigation when the patient was admitted during ketosis, before the inception of insulin therapy, and a further sample two months after the cessation of insulin injections, in the phase of remission.

Determination of Insulin Activity.—The insulin activity of serum samples was investigated by determining the effects of serum on the glucose uptake of the isolated rat diaphragm *in vitro*, employing methods previously described (Randle, 1954, 1956). In these experiments serum was diluted 1:4 with bicarbonate-buffered saline (Gey and Gey, 1936) so as to give a final glucose concentration in the incubation medium for diaphragms of 250 mg./100 ml. Glucose uptake was calculated as milligrams of glucose disappearing from the medium/g. of wet diaphragm/hour of incubation. Mean uptakes of glucose for each group of hemidiaphragms in the test were calculated and the significance of differences between means was determined by calculating "t." Reference to tables (Fisher and Yates, 1943) enabled "P," the probability that such differences were due to chance, to be determined.

Fractionation of Serum Proteins.—Serum proteins derived from blood taken during ketosis were fractionated by zone electrophoresis on columns of treated cellulose, by methods already described (Randle and Taylor, 1958a). The concentration of protein in the eluate from such columns was determined by measuring the optical density of 4-ml. portions of the eluate at 280 mμ in a Beckman spectrophotometer. The pattern of serum-protein fractions obtained in this way is shown diagrammatically in the Chart. Fractions



Subdivision of protein fractions after zone electrophoresis of serum taken during ketosis. (For further details, see text.)

were pooled, as shown, so as to yield four main subfractions. These have been designated an albumin and α_1-globulin fraction, an α_2-globulin fraction, a β-globulin fraction, and a γ-globulin fraction. Such pooled fractions were dialysed against distilled water, lyophilized, and the freeze-dried material dissolved in buffered glucose, to correspond with 50% serum, in order to test on the diaphragm for insulin activity.

Results

In Table I are shown the effects of the patient's whole serum on the glucose uptake of the isolated rat diaphragm. Serum taken during the phase of ketosis appears to be without effect on glucose uptake, though a statistically significant effect due to the serum taken in remission is seen. Reasons have been given elsewhere for regarding the effects of whole serum on glucose uptake of the rat diaphragm as due entirely to insulin (Taylor and Randle, 1959), and it is clear that during remission the patient's serum contained endogenous insulin, probably in considerable quantity.

The absence of a stimulatory effect on glucose uptake due to serum taken during ketosis does not, however, mean that there is no insulin present, since the effects of insulin, under these circumstances, might be nullified by insulin antagonists. In an attempt to separate insulin from such antagonists, serum proteins were fractionated by zone electrophoresis, and the resultant fractions also tested for their effects on the glucose uptake of rat diaphragm. These results are shown in Table II. Stimulatory effects on

TABLE I.—*Effect of Patient's Serum on Glucose Uptake of Isolated Rat Diaphragm in Vitro*

Source of Serum Sample	Addition to Medium	Glucose Uptake. Mean±S.E.M. (mg. Glucose/g. Wet Diaphragm/hr. Incubation)	Significance of Differences between Means (P)
During ketosis ..	None	3·4±0·27 (5)	<0·6>0·5
	Serum	3·6±0·21 (5)	
,, remission ..	None	2·5±0·25 (5)	<0·02>0·01
	Serum	3·6±0·23 (6)	

Serum was tested as 25% serum, in bicarbonate-buffered glucos e (see text). Number of observations is given in parenthesis after each mean .

TABLE II.—*Effect of Protein Fractions of Serum, Taken During Ketosis, on Glucose Uptake of Isolated Rat Diaphragm in Vitro*

Addition to Medium	Glucose Uptake. Mean±S.E.M. (mg. Glucose/g. Wet Diaphragm/hr. Incubation)	Significance of Differences between Means (P)
None	(a) 3·6±0·22 (6)	(b–a)<0·2 >0·1
Fraction 1 (albumin+a_1-globulin)	(b) 4·3±0·34 (5)	(a–c)<0·2 >0·1
,, 2 (a_2-globulin) ..	(c) 3·2±0·18 (5)	(b–c)<0·02>0·01
None	(a) 2·8±0·23 (5)	(b–a)<0·02>0·01
Fraction 3 (β-globulin) ..	(b) 3·9±0·23 (5)	(c–a)<0·01>0·001
,, 4 (γ-globulin) ..	(c) 3·3±0·21 (5)	

Fractions, which were prepared by zone electrophoresis, are as defined by the chart.
Each main subfraction was dissolved in a volume of buffer so as to correspond with 50% serum.
Number of observations is given in parenthesis after each mean.

glucose uptake are seen both due to the albumin-α_1 fraction and due to the β- and γ-globulins. Evidence has been presented that both these effects are due to insulin (Randle and Taylor, 1958b). It is concluded, therefore, that, even in ketosis, insulin is present in this patient's serum.

A small though not statistically significant inhibition of glucose uptake was observed due to the α_2-globulins. This effect, which may have been reduced by insulin contamination from neighbouring fractions, is referred to below.

Discussion

In view of the almost complete remission seen in this patient, the detection of insulin even during ketosis is not perhaps surprising. By contrast, Baird and Bornstein (1957, 1959) have reported that some young severe diabetics exhibited no demonstrable insulin in their serum when this was extracted by an acid-butanol type of method. It is to be presumed that these patients represent a further stage in the progression of the disease, in which the pancreatic supplies of insulin have become exhausted (cf. Wrenshall, Bogoch, and Ritchie, 1952).

Nevertheless, the possibility remains that many severe young diabetics possess adequate quantities of circulating insulin, at least in the early stages of the disease, before a state of "absolute diabetes" (Lawrence, 1951) has become established. This conclusion is also suggested by the histological studies of

Maclean and Ogilvie (1959) on the pancreases of diabetics dying within eight weeks of the onset of the disease. In such individuals these workers showed that islet tissue might be normal or hyperplastic, in contrast to that obtained from subjects dying many months or years after onset, in whom islet-cell volume was diminished.

The results presented in this paper also support the view that in diabetic ketosis there is present a circulating insulin antagonist. Many other workers have presented evidence for the presence of such antagonists in the blood of uncontrolled human diabetics (Vallance-Owen, Hurlock, and Please, 1955; Baird and Bornstein, 1957; Vallance-Owen, Dennes, and Campbell, 1958; Field, Tietze, and Stetten, 1957), though the precise identity of such substances is at present uncertain. In this connexion the small degree of inhibition of glucose uptake due to the α_2-globulins of this patient is of interest. Similar effects due to the α_2-globulins of normal human serum, whether these were prepared by cold ethanol fractionation (Taylor, Vargas, and Randle, 1959) or by column electrophoresis of serum proteins (Randle and Taylor, 1958a), have also been reported. Though it is at present uncertain to what extent this last factor is of importance in human diabetes, evidence is accumulating that it may be pituitary-dependent (Taylor, Randle, and Vargas, 1960). If this is so, then growth hormone may well be implicated in some way in the genesis of human diabetes in giving rise to such a substance which opposes the action of insulin, as Young (1951) has suggested. Similar considerations would also apply to the albumin antagonist of Vallance-Owen, Dennes, and Campbell (1958), which it has also been shown is pituitary-dependent. A further point of some practical significance emerges in that if insulin is still being secreted in the early stages of acute diabetes, what active steps should be taken to conserve actively functioning islet tissue before irreversible damage takes place. To answer this question satisfactorily there is clearly an urgent need for extensive studies on this type of patient.

Summary

A case of severe diabetes in a young adult is described, presenting with ketosis, in whom apparent clinical remission took place.

Serum insulin studies have suggested that in the initial ketotic phase insulin was present, though its effect was masked by the presence of an antagonist. With remission of the diabetes the insulin antagonism disappeared.

The possible bearing of these findings on some aspects of the aetiology of human diabetes is discussed briefly.

I thank Professor F. G. Young, F.R.S., and Dr. P. J. Randle for much help, encouragement, and valuable criticism while this work was being performed. I am indebted to Dr. Leslie Cole for making available facilities for me to work on a patient under his care, and for his own criticisms and advice. I also thank Dr. T. B. Anderson and Dr. D. G. Beynon for help with some aspects of the patient's care, Mr. S. H. H. Davison for the blood-sugar estimations, and Mrs. W. Thorne for skilled technical assistance. The cost of these investigations was in part defrayed by a grant from the British Diabetic Association.

ADDENDUM.—While this paper was in preparation, observations became available on circulating insulin in the serum of an insulin-resistant patient who also showed remission (Joslin, Root, White, and Marble, 1959). In this patient, who was maintained on a very small dose of injected insulin, whole serum, taken in remission, exhibited considerable insulin-like activity, as measured by effects on $^{14}CO_2$ production in the rat epididymal fat pad. These observations are in keeping with results presented in this paper.

REFERENCES

Baird, C. W., and Bornstein, J. (1957). *Lancet*, **1**, 1111.
—— —— (1959). *J. Endocr.*, **19**, 74.
Field, J. B., Tietze, F., and Stetten, D., jun. (1957). *J. clin. Invest.*, **36**, 1588.
Fisher, R. A., and Yates, F. (1943). *Statistical Tables*, 2nd ed. Oliver and Boyd, London.
Gey, G. O., and Gey, M. K. (1936). *Amer. J. Cancer*, **27**, 45.
Goadby, H. K. (1943). *Acta med. scand.*, **115**, 247.
Harwood, R. (1957). *New Engl. J. Med.*, **257**, 257.
Joslin, E. P., Root, H. F., White, P., and Marble, A. (1959). *The Treatment of Diabetes Mellitus*, p. 216. Lea and Febiger, Philadelphia.
Lawrence, R. D. (1951). *Brit. med. J.*, **1**, 373.
Maclean, N., and Ogilvie, R. F. (1959). *Diabetes*, **8**, 83.
Paton, A. (1959). *Brit. med. J.*, **2**, 20.
Peck, F. B., jun., Kirtley, W. R., and Peck, F. B., sen. (1958). *Diabetes*, **7**, 93.
Phillips, W. (1957). *Lancet*, **1**, 281.
Randle, P. J. (1954). *Brit. med. J.*, **1**, 1237.
—— (1956). *J. Endocr.*, **14**, 82.
—— and Taylor, K. W. (1958a). Ibid., **17**, 387.
—— —— (1958b). *Lancet*, **2**, 996.
Stutman, L. J., and Hayes, J. D. (1959). *Diabetes*, **8**, 189.
Taylor, K. W., and Randle, P. J. (1959). *J. Endocr.*, **19**, 221.
—— —— and Vargas, L. (1960). *Lancet*. In press.
—— Vargas, L., and Randle, P. J. (1959). *Biochem. J.*, **73**, 12P.
Vallance-Owen, J., Dennes, E., and Campbell, P. N. (1958). *Lancet*, **2**, 336.
—— Hurlock, B., and Please, N. W. (1955). Ibid., **2**, 583.
Waddell, W. B. (1959). *Brit. med. J.*, **1**, 1120.
Wolff, F. (1959). Ibid., **1**, 1473.
Wrenshall, G. A., Bogoch, A., and Ritchie, R. C. (1952). *Diabetes*, **1**, 87.
Young, F. G. (1951). *Brit. med. J.*, **2**, 1167.

HYPOTHERMIC COMA IN MYXOEDEMA

BY

J. H. ANGEL, M.D., M.R.C.P.
Senior Medical Registrar, Whittington Hospital, London

AND

L. SASH, M.B., B.Ch., D.C.H.
Medical Registrar, Edgware General Hospital, London

Though coma in myxoedema has been described with increasing frequency during the past six years, the condition has received only grudging recognition in the standard textbooks. The 1959 edition of Cecil and Loeb's *Textbook of Medicine* makes no reference to it, while the 1956 edition of Price's *Textbook of the Practice of Medicine* mentions it only in passing. This paper describes three further cases. Two of the patients died during their first episode of coma; the third recovered from quite a deep coma on two separate occasions.

Case 1

A housewife aged 56 was admitted to hospital on January 16, 1959, complaining of progressive swelling of the feet for the previous six weeks. On further questioning, she admitted to some shortness of breath and to abdominal discomfort and distension. She had not suffered from angina of effort and had been able to carry out her normal household duties. For a year before her admission she had noticed that her voice was becoming gruff and that her hair was falling out.

On examination she was jovial and co-operative, though slow. Her eyebrows were absent, the scalp hair was coarse, and axillary and pubic hair was scanty. Her eyes were puffy; the skin was dry and coarse in texture, and cold. Her heart was fibrillating at 60 a minute; the heart sounds

were faint; and blood-pressure was 190/120. She was in congestive cardiac failure with a raised jugular venous pressure, ascites, and oedema of the legs and feet. The tendon reflexes were diminished and the plantar responses equivocal.

Investigations.—Haemoglobin, 83%; W.B.C., 5,400; serum cholesterol, 145 mg./100 ml.; basal metabolic rate, −42 and −50%. Electrocardiogram showed atrial fibrillation at a slow rate (varying from 40 to 60 a minute). Chest radiograph showed generalized cardiac enlargement. Temperature taken on an ordinary clinical thermometer did not register more than 96° (35.6° C.) at any time.

Myxoedema and congestive cardiac failure were diagnosed and digoxin and mercurial diuretics given. Treatment with thyroid extract ½ gr. (32 mg.) b.d. was started on January 23, when the investigations were complete. Two days later the patient complained of severe burning sensations throughout her body: these were associated with some disorientation. She had been constipated before admission, but her bowels became regular when thyroid treatment was given.

On January 29 she became drowsy for the first time. Her temperature had not responded to treatment, a low-reading thermometer showing 85° F. (29.5° C.). It was thought that she was slipping into coma; therefore 5 μg. of triiodothyronine intramuscularly was given each day, and the bed warmed with an electric blanket. By February 2 she was comatose. She was given gr. 5 (0.32 g.) of thyroid extract intramuscularly, followed by gr. 2½ (0.16 g.) 12-hourly. Prednisolone, 5 mg. b.d., was added in an effort to counter any concurrent adrenal insufficiency. None of these measures was of any avail. On February 3 she was given two 25-μg. doses of triiodothyronine intravenously, but she died later that evening. Permission for necropsy was not granted.

Case 2

A housewife aged 78 was admitted to hospital on January 27, 1959. She was reluctant to walk or speak, and a history was obtained from her daughter-in-law. She had been deaf for many years and had become increasingly apathetic during the past few years. Severe constipation had been a troublesome feature. She had become very intolerant of cold, was losing her hair, and her speech had become slow and slurring. She had recently developed weakness of the right side of the body.

On examination she appeared pale and completely passive. Her speech was very slow, slurred, and unintelligible. Her skin was cold; her facial appearance greatly resembled that of Case 1. The pulse rate was 36 and B.P. 150/80. There was no evidence of congestive failure or any cardiac lesion. There was evidence of right hemiparesis, and the right plantar reflex was extensor.

Investigations.—The temperature, taken by an ordinary clinical thermometer, never rose above 95° F. (35° C.). A low-reading thermometer showed it to be 85° F. (29.5° C.). Hb, 87%; W.B.C., 16,600; blood urea, 26 mg./100 ml.; serum cholesterol, 293 mg./100 ml. The urine showed considerable proteinuria. Moderate cardiac enlargement was seen on the chest radiograph. Electrocardiogram showed atrial fibrillation at a very slow rate, varying from 25 to 40 per minute.

Treatment was immediately started with thyroid ¼ gr. (16 mg.) b.d., increasing to 1 gr. (65 mg.) daily on January 30. On this day her condition deteriorated and she became semiconscious. Triiodothyronine, 100 μg. six-hourly, was given by mouth and she was warmed by means of an electric blanket, but without avail. On January 31 thyroid extract, 0.5 ml. intramuscularly 12-hourly, was given, but she died late than evening. Permission for necropsy was not granted.

Case 3

A woman aged 82 was admitted to hospital on March 21, 1958, because of recent melaena. She appeared very pale. Her hair was dry, her skin coarse, her tongue thick and protruding, and her voice croaky.

A diagnosis of gastro-intestinal bleeding and probable myxoedema was made; since the haemoglobin had fallen to 18% it was decided to give a transfusion before carrying out any further investigations. She received 4 pints (2.3 litres) of packed cells over the next 24 hours and the haemoglobin rose to 79%. On March 23 she was drowsy. Next day this was more pronounced and her response to questions or other other stimuli was very slow. The rectal temperature was 95° F. (35° C.); serum cholesterol, 134 mg./100 ml. She was thought to be in incipient myxoedematous coma and was given 50 μg. of triiodothyronine intravenously. On the next two days she was given further intravenous injections of 100 μg. of triiodothyronine. By March 26 she was much livelier and was maintained on an oral dose of 20 μg. of triiodothyronine daily. Serial electrocardiograms showed an increase in the rate and in the amplitude of the complexes. She was discharged home on April 16.

Nine days later (April 25) she was readmitted because she had become semi-stuporous at home. Her pulse rate was 52, rectal temperature 96.2° F. (35.7° C.). The E.C.G. showed very low voltage curves once more. It was found that she had taken only a few of the triiodothyronine tablets given to her when discharged from hospital. She was therefore treated again as a case of myxoedematous coma and given triiodothyronine, 100 μg. intravenously. She became more active after this and was put on a maintenance dose of 20μg. daily. Further intravenous injections of 100 μg. were given on April 28 and May 5. Treatment was later changed to thyroid extract, and she was sent home on May 23 on 1½ gr. (0.1 g.) b.d. The electrocardiographic complexes were of normal amplitude by the time she was discharged for the second time.

Apart from short admissions to hospital occasioned by fractures of her ribs in December, 1958, and by a Colles fracture of her right wrist in January, 1959, she remained well during the next few months. But after a time she gave up taking her thyroid tablets and on May 25, 1959, she was readmitted to hospital, having greatly deteriorated both mentally and physically. Treatment with thyroid, ¼ gr. (32 mg.) daily, resulted in a remarkable improvement. She died quite suddenly on June 26.

Necropsy (Dr. A. B. Bratton).—The body was that of a wasted, frail old woman. There were numerous pigmented warts on the skin of the abdomen. Thoracic kyphosis was marked. The myocardium showed oedema and brown atrophy. There was moderate atheroma of the coronary arteries, with a thick button almost blocking the anterior descending branch. In the remainder of the arterial tree was a more severe degree of atheroma. The lungs showed atrophic emphysema. In the pyloric portion of the stomach an ulcerated carcinomatous plaque was found, 5 cm. in diameter: its base was continuous with a mass of glands 1.5 cm. in diameter. The intestines were slightly oedematous. The liver showed oedema and brown atrophy and contained deposits of secondary carcinoma up to 4 cm. in diameter. Both lobes of the thyroid were fibrotic. The suprarenal cortex was well developed. There was atrophy of the ovaries and uterus, the latter containing a few fibromyomata up to 1.25 cm. in diameter. Oedema and atrophy of the spleen, kidney, and pancreas were found.

Histology.—The thyroid gland showed extreme fibrosis and slight lymphoid filtration. A columnar-cell carcinoma infiltrated all coats of the stomach, with an abscess beneath the peritoneum and secondary deposits in the liver.

Discussion

By the end of 1958 22 cases of myxoedematous coma had been described in the literature. Most of these were associated with hypothermia. In order to recognize a hypothermic state a low-reading thermometer must be used, since the standard clinical thermometer records to only 95° F. (35° C.) (Sheehan and Summers, 1952). In only one case (Karhausen and Zylberszac, 1955) has the temperature in terminal myxoedema coma been

Details of Recent Cases

Author	Case	Age and Sex	Temperature °F.	Temperature °C.	Serum Cholesterol (mg./100 ml.)	Treatment: Rewarming	Thyroid	Thyroxine	Triiodothyronine	A.C.T.H. or Cortisone	Result
Le Marquand *et al.* (1953)	1	61 F	95–97	35–36·1	390	No	—	—	—	Adrenal cortical extract 10 ml. 4-hourly	Died in 4 days
	2	50 F	95	35	495	,,	—	10 mg.	—	—	,, ,,21 ,,
,, (1955)	3	70 F	74	23·3	560	Yes	—	0·5 mg. i.v.	—	25 mg. i.m. 4-hourly	,, ,, 2 ,,
Summers (1953)	4	59 M	83	28·3	—	No	1 gr. (65 mg.) t.d.s.	1 mg. s.c. 6-hourly	—	—	,, ,, 4 ,,
	5	65 F	75	23·9	—	Yes	—	2 mg. s.c. 6-hourly	—	—	,, ,,24 hours
	6	63 M	91·4	33	—	,,	1 gr. (65 mg.) t.d.s.	2 mg. 6-hourly	—	D.C.A. 10 mg. and cortisone 100 mg. by i.v. drip	,, ,, 2 days
	7a	59 M	96–98	35·6–36·7	—	No	—	1 mg. 6-hourly	—	—	Recovered
	7b	59 M	83·5	28·6	—	,,	—	1 mg. 6-hourly	—	Cortisone 100 mg. 6-hourly	Died in 2 days
Malden (1955)	8	60 F	95–97	35–36·1	242	,,	2½ gr. (0·14g.) in all	—	—	—	,, ,,36 hours
	9	64 F	78	25·6	388	Yes	¼ gr. (16 mg.) b.d.	—	—	D.C.A 10 mg. Adrenal cortical extract 30 ml.	,, ,,20 ,,
	10	62 F	Unrecordable on clinical thermometer		538	,,	—	0·025 mg. i.v. 0·3 mg. daily 0·6 mg. ,,	—	A.C.T.H. 10 mg. i.v., then 25 mg. i.m. b.d.	Recovered
	11	67 F	80	26·7	—	—	—	—	—	—	Died
Karhausen and Zylberszac (1955)	12	63 F	100·4	38	336	Not necessary	—	1 mg. i.v.	—	Cortisone 100 mg. orally	,,
Reid (1955)	13	63 F	96–97·4	35–6·36·3	660	Yes	½ gr. (16 mg.) b.d.	0·1 mg. b.d.	—	"Eucortone" 20 ml. i.v., D.C.A. 20 mg.	Died in 3 days
Levin and Daughaday	14	41 F	97·8	36·6	450	?	—	DL-Thyroxine 0·2 mg. i.v. 1 gm. i.v.	—	Hydrocortisone. Cortisone	,, ,,48 hours
Marshall and McCaughey (1956)	15	70 F	74	23·3	293	Yes	No thyroid at all given			Delta-cortisone 60 mg. Cortisone 100 mg. daily by mouth	,, ,, 7 days
Dyson and Wood (1956)	16	70 F	82	27·8	393	,,	—	0·1 mg. orally 0.025 mg. i.v.	1·2 mg. i.v. 1 mg.i.v. 0·5 mg. i.v. 0·3 mg. i.v.	Hydrocortisone intravenously for first 3 days	,, ,, 5 ,,
Anderson and Hausmann (1956)	17	49 M	84	28·9	—	?	—	0·2 mg. orally	0·05 mg. i.v.		,, ,, 3 ,, (? coronary thrombosis)
Curtis (1956)	18	60 F	Not stated		483		1/10 gr. (6·5 mg.) Jan. 22 ¼ gr. (16 mg.) Jan. 23			A.C.T.H. 25 units i.v. for 2 days. 160 units Jan. 21	Died in 2 days
Macdonald (1958)	19	19 M	82	27·8	200	Yes	—	0 02 mg. 4-hourly sub-lingually	—	Hydrocortisone 100 mg. i.v. for 12 hours. Cortisone 50 mg. i.m.	,, ,, 3 ,,
	20	80 F	97	36·1	—	,,	—	0·05 mg. 4-hourly sub-lingually	—	Cortisone 50 mg. 4-hourly i.m.	,, ,, 12 hours
	21	79 F	91	32·8	200	No	—	—	0·08 mg. i.v. 0·02 mg. sub-lingually 4-hourly 0·08 i.v. next day and on 3rd day	Cortisone 50 mg. i.m. 4-hourly	Recovered. Later treated with oral thyroxine and thyroid
Surtees and Ginsberg (1958)	22	69 F	87	30·6	645	Yes	—	—	0·1 mg. intragastric 0·04 mg. b.d. 0·02 mg. daily	—	Recovered (but died 3 weeks later of myocardial infarction)
Nieman (1959)	23	62 F	76	24·4	440	,,	—	—	0·1 mg. intragastric drip	Hydrocortisone 100 mg. i.v.	Died in 24 hours
	24	49 F	96	35·6	140	No	Given by Ryle tube. Dose not stated	—	—	—	Recovered
Present series Case 1	25	56 F	85	29·5	145	Yes	2½ gr. (0·16 g.) 12-hourly i.m.	—	0·005 mg.i.m. 0·025 mg. i.v.	Prednisone 5 mgm. b.d.	Died in 5 days
,, 2	26	78 F	85	29·5	293	,,	,, ,,	—	0·1 mg. 6-hourly by mouth	—	,, ,, 2 ,,
,, 3	27a	82 F	95	35	134	No	1½ gr. (0·1 g.) b.d. after recovery	—	0·05 mg. i.v. 2 doses of 0·1 mg. i.v. then orally 0·02 mg. daily	—	Recovered
	27b	82 F	96·2	35·7	168	,,	1½ gr. (0·1 g.) b.d. full recovery	—	0·1 mg. i.v. daily	—	,,

raised. Clinical details of the cases described in the past few years and of their treatment are given in the Table.

Since myxoedematous coma is caused directly by lack of thyroid hormone, and since its most striking clinical manifestation is the corpse-like coldness of the body, it would appear logical to treat patients by administering the most rapidly effective thyroid hormone and rewarming them. In spite of the application of these measures to a greater or less extent, all but 6 of the 27 patients described in the literature have died while still in coma. The purpose of this publication is to analyse more closely the factors which have resulted in the recovery of the five successfully treated cases.

Differing opinions have been offered on the value of rewarming the patient. Macdonald (1958), for example, has stated that it is illogical and probably dangerous. The methods employed for the purpose have included immersion in a warm bath, the use of heat cradles, and the use of electric blankets. Of the six patients who recovered from myxoedematous coma, only two were rewarmed (Malden, 1955—Case 3; Surtees and Ginsberg, 1958), the first by electric blankets and the second by means of a heat cradle.

Experiments in rats have shown that the requirements of the organism for thyroid hormone increase as the environmental temperature falls (Dempsey and Astwood, 1943). Similarly, exposure of rats to a high temperature reduces the requirement for thyroid hormone. There are good grounds for keeping the dose of thyroid hormone administered to patients in myxoedematous coma as low as possible. Most cases occur during the winter months, usually at a time when the temperature even of hospital wards has fallen below the optimal. With these factors in mind, we feel that rewarming is advisable. It should, however, be gradual, otherwise cutaneous vasodilatation will defeat its whole purpose. Rewarming in itself will not bring the patient out of coma.

Thyroid Hormones

Thyroxine.—L-Thyroxine occurs naturally in the thyroid gland. A single intravenous dose given to patients with myxoedema produces some effect on the basal metabolic rate in six to eight hours, but the maximal effect is not reached until 8 to 10 days (Blackburn *et al.*, 1953). When treatment with thyroxine is discontinued in established cases of myxoedema the basal metabolic rate does not return to its original level for several weeks. L-Thyroxine is 8 to 10 times as active as the D-thyroxine. Chemists still occasionally supply D-thyroxine; this may explain the occasional failure of treatment of myxoedematous patients with thyroxine (Goolden and Burrell, 1957) and possibly the failure to recover from coma (Levin and Daughaday, 1955).

Triiodothyronine.—This hormone was first shown to be useful in the treatment of myxoedema by Gross *et al.* (1952). Its action is more rapid and less prolonged than that of thyroxine. Oral administration increases the basal metabolic rate of myxoedematous patients within a few hours, maximal at the eighth to twelfth hours (Ibbertson *et al.*, 1959). A similar rapid action has been demonstrated after an intravenous dose. If the hormone is withdrawn from hypothyroid patients the basal metabolic rate returns to its pre-treatment level in seven to nine days (Lerman, 1953). The daily replacement dosage for myxoedematous patients has been estimated at 0.07–0.1 mg. (Selenkow and Asper, 1955).

Triiodothyroacetic Acid (Triac).—This is a synthetic hormone which appears to act a little more rapidly than triiodothyronine. In patients with a past history of angina even small doses may precipitate cardiac pain; its use should therefore be avoided in such cases. However, in the treatment of myxoedematous coma in patients known not to have suffered previously from anginal pain triac has been held to be the drug of choice (Ibbertson *et al.*, 1959). The daily replacement dosage is 4–6 mg. The drug is not generally available.

The rate of response to these rapidly acting thyroid hormones appears to depend on the duration of the previous hypothyroidism. The two patients in Ibbertson's series showing the slowest response to oral triiodothyronine and to triac were both previously untreated. One was a case of primary myxoedema, the other of hypopituitarism with complete thyroid failure, and both were of long standing. Since myxoedematous coma mostly occurs in previously undiagnosed cases, the response to the first dose of hormone will be delayed. This suggests that the initial dose should be larger than the usual replacement dose, and favours the use of the more rapidly acting triac.

Of the six successfully treated patients, one was treated with thyroid extract via a Ryle tube, two were given thyroxine, either intravenously or orally (Malden, 1955, Case 3; Summers, 1953, Case 4), and three received triiodothyronine. Surtees and Ginsberg (1958) gave their patient 0.1 mg. of triiodothyronine by intragastric drip, followed by 0.04 mg. twice daily. Macdonald's patient received 0.08 mg. intravenously, followed by another intravenous dose of 0.08 mg. 12 hours later. She relapsed into coma 48 hours after admission and received a further dose of 0.08 mg. intravenously; from then on she made an uninterrupted recovery. Our own patient was treated with an initial intravenous dose of 0.05 mg., followed by 0.1 mg. intravenously on each of the two subsequent days. When she relapsed she again received 0.1 mg. intravenously.

Though most writers now agree that triiodothyronine is the most effective hormone in the treatment of myxoedematous coma, there is much disagreement about the dosage and the method of administration. This stems from the very powerful effect upon the heart exerted by thyroid hormones. Several of the patients referred to in this review have died of myocardial infarction shortly after administration of a thyroid hormone. Indeed, Goolden and Burrell (1957) have gone so far as to state that the majority of patients in myxoedematous coma treated with thyroid hormone have deteriorated further. On these grounds they have advocated very cautious dosage (0.01 mg. every 12 hours by intravenous injection, the dose later to be modified according to the response). Martin (1958) suggests 0.02 mg. six-hourly by intramuscular injection. At the other end of the scale, Spence (1959) considers the correct dose to be of the order of 0.1 to 0.25 mg. 12-hourly by intravenous injection. Dyson and Wood (1956) gave 1.2 and 1 mg. intravenously, but their patient died.

In order to chart a course between the Scylla of undertreatment and the Charybdis of myocardial infarction and acute heart failure, we would suggest that, for patients *known not to have suffered from angina previously*, an initial dose of 0.08 mg. of triiodothyronine intravenously be given, and that it should be given as soon as any drowsiness becomes manifest. A maintenance dose of 0.05–0.1 mg. intravenously at 12-hourly

intervals should be given until consciousness returns, after which the hormone may be administered by mouth (0.02 mg. four- to six-hourly). In patients with a past history of angina, the initial dosage must be more cautious (0.01–0.02 mg. intravenously); the later dose will be governed by the response and by the presence or absence of anginal pain.

Macdonald (1958) has suggested that hypothermia in itself is an indication to start treatment even if coma does not appear imminent. He also considers that the dose of triiodothyronine should be proportional to the degree of hypothermia. We feel that the fate of our first two patients bears out these suggestions and that we should have instituted more vigorous treatment at an earlier stage of their stay in hospital. Both were conscious on admission; Case 1 was quite lively and jovial. Yet in both the body temperature was well below normal. Both lapsed into coma though treatment with a slow-acting thyroid preparation had already been started. Case 1, for example, had received a total of 6 gr. (0.4 g.) of thyroid extract over a period of six days at the time that she became comatose. It seems to us that the use of triiodothyronine by mouth after admission to hospital might well have saved the life of both these patients.

The fate of these two patients also suggests that one should not spend too long carrying out investigations on myxoedematous patients, especially during the winter months.

Corticosteroids

Many patients with myxoedema show an impairment of adrenocortical function which is reflected in their lowered urinary 17-hydroxycorticoid output. The treatment of hypopituitarism associated with complete thyroid failure ("hypopituitary myxoedema") by thyroid extract has in the past led to a sudden adrenal crisis. For these reasons many physicians have advocated the use of corticotrophin or of corticosteroid hormones in the initial treatment of severe cases of myxoedema, whether primary or secondary.

Steroid therapy was employed in only two of the six successfully treated cases of myxoedematous coma. Corticotrophin was given by intravenous infusion in Malden's case, and cortisone was administered four-hourly in a dosage of 50 mg. intravenously by Macdonald.

It would appear that corticosteroid therapy is not essential to recovery in myxoedematous coma. However, no harm appears to have resulted from its use in the unsuccessfully treated cases. In a seriously ill patient, many will feel that no form of therapy that may possibly do good should be withheld, and will administer steroids on these grounds alone. If there is obvious evidence of electrolyte disturbance or of hypoglycaemia, then the indications for steroid therapy will be clear-cut.

Other Measures

Antibiotic Cover.—Patients in coma are always liable to develop a fatal pneumonia. Antibiotic cover should therefore always be given.

Artificial Ventilation.—The respiratory rate in patients in myxoedematous coma often becomes very slow. This may lead to carbon-dioxide retention and a severe respiratory acidosis. Nordqvist *et al.* (1959) described two such cases whose serum pCO_2 rose to 86 and 109 mm. Hg respectively. They treated their patients by tracheal intubation and artificial ventilation with mask and bag; this proved insufficient, and the patients were put into a respirator for two weeks until the carbon-dioxide tension could be maintained at a normal level.

It has been shown that acute carbon-dioxide retention with an increase of carbon-dioxide tension to values over 70 mm. Hg may exert a considerable depressant effect on the myocardium. If the presence of carbon-dioxide retention in myxoedematous coma is confirmed by other workers, its prevention and treatment will obviously play an important part in the treatment of the coma.

Summary

Three further cases of myxoedematous coma are described; one of them is the sixth case reported to have survived the acute episode. The treatment of the condition in previously published cases is reviewed and discussed.

It is suggested that patients with myxoedema should not undergo investigations for overlong periods, especially during the winter months. Cases of severe myxoedema may lapse into coma even after treatment with thyroid extract has started. We would agree with a previous suggestion that hypothermia, in itself, is an indication for immediate treatment with a rapidly acting thyroid hormone.

We are grateful to Drs. L. I. M. Castleden, T. St. M. Morris, and A. N. Exton-Smith for permission to report on cases under their care.

References

Anderson, A., and Hausmann, W. (1956). *Lancet*, **2**, 999.
Blackburn, C. M., McConahey, W. M., Keating, F. R., and Albert, A. (1953). *J. clin. Endocr.*, **13**, 852.
Curtis, R. H. (1956). *Ann. intern. Med.*, **44**, 376.
Dempsey, E. W., and Astwood, E. B. (1943). *Endocrinology*, **32**, 509.
Dyson, A., and Wood, M. W. W. (1956). *Lancet*, **2**, 757.
Goolden, A. W. G., and Burrell, C. D. (1957). *Brit. med. J.*, **2**, 1028.
Gross, J., Pitt-Rivers, R., and Trotter, W. R. (1952). *Lancet*, **1**, 1044.
Ibbertson, K., Fraser, R., and Alldis, D. (1959). *Brit. med. J.*, **2**, 52.
Karhausen, L., and Zylberszac, S. (1955). Ibid., **2**, 766.
Le Marquand, H. S., Hausmann, W., and Hemsted, E. H. (1953). Ibid., **1**, 704.
—— —— —— (1955). Ibid., **2**, 773.
Lerman, J. (1953). *J. clin. Endocr.*, **13**, 1341.
Levin, M. E., and Daughaday, W. H. (1955). *Amer. J. med.*, **18**, 1017.
MacDonald, D. W. (1958). *Brit. med. J.*, **2**, 1144.
Malden, M. (1955). Ibid., **2**, 764.
Marshall, R. J., and McCaughey, W. T. E. (1956). *Lancet*, **2**, 754.
Martin, L. (1958). *Practitioner*, **180**, 50.
Nieman, E. A. (1959). *Brit. med. J.*, **1**, 1204.
Nordqvist, P., Dhuner, K. G., Sternberg, K., and Örndahl, G. (1959). Ibid., **1**, 234.
Reid, A. W. (1955). Ibid., **2**, 967.
Selenkow, H. A., and Asper, S. P. (1955). *J. clin. Endocr.*, **15**, 285.
Sheehan, H. L., and Summers, V. K. (1952). *Brit. med. J.*, **1**, 1214.
Spence, A. W. (1959). Ibid., **1**, 706.
Summers, V. K. (1953). Ibid., **2**, 366.
Surtees, S. J., and Ginsberg, S. (1958). *Postgrad. med. J.*, **34**, 443.

Practical Dietetics is a collection of articles published in *The Practitioner* throughout 1959. The aim of the series was to provide the general practitioner with authoritative, yet practical, guides to the planning and supervision of those diets which may be necessary for his patients. The kinds of diet included are low-salt, low-fat, and low-residue diets, and the conditions for which special diets are listed include renal disease, diabetes, obesity, peptic ulcer, toxaemia of pregnancy, weaning, gastro-enteritis in children and infants, old age, and canteen diets. The booklet is edited by Dr. W. A. R. Thomson, and published by *The Practitioner* at 4s. 6d.

STUDIES IN THE EPIDEMIOLOGY OF TINEA PEDIS

III. CROSS-INFECTION IN THE FAMILY

BY

MARY P. ENGLISH, M.Sc.
Medical Mycologist, Bristol Royal Hospitals

AND

MARY D. GIBSON, M.B., Ch.B., D.P.H.
Assistant Medical Officer of Health, Bristol

A survey of tinea pedis in day-school children in Bristol (English and Gibson, 1959a) showed *Trichophyton mentagrophytes* to be responsible for 84.4% of the cases, and it was later demonstrated that public swimming-baths were probably an important means of transmission of this fungus among school children (English and Gibson, 1959b). Obviously it was also possible that children might become infected from a source within their families, so we arranged to visit the households of some infected children.

In a previous survey of families in the Bristol area (English, 1957) it had been shown that when tinea pedis was caused by *T. rubrum* cross-infection within the family was important. We have not been able to find any report of a planned investigation into the behaviour of *T. mentagrophytes* in a group of families, though reports of the spread of both this fungus and *T. rubrum* in single families have followed the 1957 survey (Ingram and La Touche, 1957; Rothman and Windhorst, 1957).

In the *T. rubrum* family survey the original case in each family was usually an adult who had been referred to a dermatologist because of established tinea pedis of some years' duration, whereas in our proposed survey of the families of school children the first case in the family to come to our notice would be the child—in most cases asymptomatic and unaware of the infection and not under treatment at the time of the survey. Thus a comparison of these two groups would not be valid.

We have therefore included in this investigation a group of families where the original cases had been referred to a dermatologist for a *T. mentagrophytes* infection.

The Subjects

The "school families" were the families of children from one senior boys' school (No. 2 in the school survey) and one senior girls' school (No. 8 in that survey), both in district A (the district which we had found to be most heavily infected with the *interdigitale* type of *T. mentagrophytes* (English and Gibson, 1959a). Twenty-eight families were eligible, but three had left the district. The remainder were all known to one of us (M.D.G.) and were asked personally for their co-operation. This method ensured better co-operation from working-class families than we were able to obtain from those in the second group. In all, 22 families agreed to take part.

The "clinic families" were those of patients who had been referred for specialist advice in Bristol or Weston-super-Mare between 1955 and 1959. Few of these were known to us, so most were approached by letter, as in the *T. rubrum* family survey. Of 27 families, four had left the district and four refused to take part, three of the latter living in one working-class district of Bristol. In all, 19 families co-operated.

The survey was carried out between December, 1957, and May, 1959.

Terminology.—The "primary case": the first case to come to our notice in any family, whether school child or clinic patient. A "carrier": a person with no signs or symptoms of infection at the time of examination, but from whom a dermatophyte was isolated. "Bathing" and "bathed" refer to "taking a bath" *not* to "going for a swim."

Methods

The home visits were made by either or both of us; the laboratory work was the responsibility of one (M.P.E.). Methods differed from those of the *T. rubrum* survey (English, 1957) in only two ways. Scrapings were taken from all subjects, not only from those with lesions; and hands were not examined, as five years' experience in the skin clinic of Bristol General Hospital had failed to disclose a single case of *T. mentagrophytes* infection of the hands.

Cross-infection

Out of the 22 school families a single contact was infected in each of three; in 19 families no spread of infection had occurred. In the 19 clinic families spread of infection had occurred in eight and in four of these the spread was to two contacts, in the others to one (Table I).

TABLE I.—*Epidemiology of Tinea Pedis Due to T. mentagrophytes Compared with the Corresponding (1957) Results for T. rubrum*

	T. mentagrophytes				*T. rubrum* (1957)	
	School Families		Clinic Families			
	No.	%	No.	%	No.	%
Total families (=total primary cases)	22		19		18	
Families with cross-infection	3	14	8	42	8	44
Primary cases seeking specialist advice	0	0	16*	84	16*	89
Primary cases cured	19	86	6	40†	0	0
Total contacts	77		52		46	
Infected ,,	3‡	4	12§	23	11	24
Total offspring aged 12 or over of infected parents	6		16		11	
No. of such offspring infected	3	50	7	44	6	55
Total infected persons	25		31		29	
No. of toenail infections	0	0	2	6	19	66
,, ,, groin ,,	0	0	1	3	7	24
Couples with one or both partners infected	3		18		15	
Couples with both partners infected	0	0	5	28	4	27
Ratio of males to females infected	7:1		2:1		1:1	

* Remaining primary cases came to the clinic for other skin conditions and were found to have tinea pedis as well.
† 4 cases still under treatment: 6 of the remaining 15 cured.
‡ 1 case was a "carrier."
§ 2 cases were "carriers."

Within all but one of the families in which more than one person was infected with *T. mentagrophytes* the isolates were mycologically similar. In the one school family in which the isolates differed, this was in intensity of pigmentation only, and at the first subculture the difference was hardly noticeable.

For a strict comparison of cross-infection rates of the two fungi the carriers recorded in the present survey must be ignored, as no search was made for these in the *T. rubrum* survey. If this is done, a spread of infection can be recorded in only two school families,

for the carrier was the only infected contact in the third, and to 10 contacts in seven clinic families.

The average age of the primary cases in the two groups of families, and their status as determined by the Registrar-General's social classification, are compared in Table II with the figures applicable to tinea pedis abstracted from the results of the *T. rubrum* family survey.

TABLE II.—*Characteristics of the Groups of Families*

Characteristic	*T. mentagrophytes*		*T. rubrum* (1957)
	School Families	Clinic Families	
Average age of primary cases	14·5 years	38·9 years	40·6 years
No. of families in social class I	0	3	6
No. of families in social class II	3	7	5
No. of families in social class III	16	9	5
No. of families in social class IV and V	3	0	2

The close resemblance between the average age of the primary cases and the range of social class in the *T. mentagrophytes* clinic families and the *T. rubrum* families (Table II) was paralleled by the similarity of the cross-infection rate both among families and among contacts, and by the percentage of conjugal infections (Table I). The school families contrasted markedly in all these aspects. The cross-infection rates in the *T. mentagrophytes* school and clinic families, both per family and per contact, were significantly different at the 1% level.

One explanation for these differences could lie in the quick elimination of the focus of infection in the school families, as indicated by the comparatively high cure rate of the primary cases. Another could be sought in the different distribution of social class in the school and clinic groups, which could, in turn, imply different personal habits.

The *T. mentagrophytes* clinic families and the *T. rubrum* families, having been selected in the same way, are strictly comparable to one another. These two groups have therefore been combined in Table III to show the relationship of cross-infection to social class.

TABLE III.—*Relationship of Cross-infection to Social Class in Combined T. mentagrophytes Clinic and T. rubrum Families*

	Social Class			
	I	II	III	IV and V
No. of families	9	12	14	2
,, with cross-infection	7 (78%)	6 (50%)	3 (21%)	0

Cross-infection in the home would be most likely to occur in the bathroom, and the greater the frequency of bathing the greater the risk would be. All *T. mentagrophytes* families, except two without bathrooms, were therefore circulated with questionaries asking how many baths per week were taken by each member. Replies were received from 16 clinic and 17 school families: all those failing to reply were in social class III. The results were classified according to school and clinic grouping and to social class. Where baths were taken more frequently in summer than in winter, the summer frequency was tabulated. A number of those who bathed only once a week stated that they washed their feet daily. We do not know to what extent this entailed standing with bare feet.

The results are shown in Tables IV and V. They offer one reasonable explanation for increase in cross-infection with rise in social class, and could therefore account for the different cross-infection rates in school and clinic families.

TABLE IV.—*Relationship of Social Class and Frequency of Bathing (Replies from 33 Families)*

No. of Baths per Week	No. of Persons in Social Class							
	I		II		III		IV and V	
	No.	%	No.	%	No.	%	No.	%
5–7	8	50	8	22	3	5	0	0
2–4	8	50	21	58	16	26	0	0
1	0	0	7	19	41	68	16	100
Total	16		36		60		16	

TABLE V.—*Frequency of Bathing in School and Clinic Families (Replies from 33 Families)*

No. of Baths per Week	No. of Persons			
	School Families		Clinic Families	
	No.	%	No.	%
5–7	3	4	16	30
2–4	16	21	29	55
1	56	75	8	15
Total ..	75		53	

A finding common to all three groups was the high risk of infection run by offspring of 12 years or over who had been brought up in infected families (Table I).

Other Observations on the T. mentagrophytes Families

The low incidence of groin infections due to *T. mentagrophytes* (Table I) is in agreement with the observations of English and La Touche (1957); and that of nail infections (Table I) is confirmed by figures for Bristol skin clinics, where, out of 70 cases of *T. mentagrophytes* infection, the nails were involved in only five.

Dermatophytes other than *T. mentagrophytes* were found only three times, two of these being concurrent infections of *Epidermophyton floccosum* in primary cases. The third was an *E. floccosum* infection in a clinic family in which no cross-infection with either fungus had occurred.

Only one home was conspicuously dirty; all but two families had bathrooms; almost all shared their bath-mat; bare feet in the house and the use of swimming-baths and non-domestic showers were uncommon except among school children. It was therefore impossible to correlate cross-infection with any of these things.

In the clinic families two males were infected for every female: this must be compared with a 7:1 sex ratio for *T. mentagrophytes* found in the school families and a 1:1 ratio in the *T. rubrum* families.

Discussion

This survey shows that, in the home, cross-infection with tinea pedis due to the *interdigitale* type of *T. mentagrophytes* is important in certain circumstances.

Sulzberger and Baer (1955), quoting evidence based on indirect methods of assessment, stated that the spread of tinea pedis in the family was negligible. The 1957 survey showed this to be untrue for *T. rubrum*, while the present survey extends that finding to *T. mentagrophytes*. Even the low cross-infection rate in school families is significantly greater than that claimed by Sulzberger and Baer for patients consulting dermatologists. The rate in the clinic families which, by their

method of selection, are directly comparable to Sulzberger's subjects, is much higher still.

However, the comparatively small degree of spread found in school families suggests that the home is not the main source of infection in day school children, though it was interesting that in the only school families where cross-infection did occur the other case was the father, and that in at least two of these three families he had apparently been infected many years before, during his war service.

There are two possible reasons for the unexpected observation of different cross-infection rates in the two groups. As we have shown, it could, at least in part, be accounted for by their different social composition and the consequent difference in bathing habits. Other differences due to social status might also be involved.

Another possible explanation, probably coexistent with the first, lies in the different character of the primary cases in the two groups. The school children were mostly unaware of their very mild infections, and 19 out of 22 were quickly cured at their school clinic. But 16 of the 19 clinic patients were sufficiently worried by the severity and long duration of their condition to seek specialist advice, and this had led to cure in less than half of those who had completed treatment.

The feet of day school children in Bristol are subjected to frequent examination by swimming instructors, school nurses, and physical education teachers. Most of those treated at school clinics, like the primary cases of the school families, therefore, probably receive treatment within a short time of becoming infected. We have no evidence of whether the ease with which most of the children were cured was due to this prompt treatment or to a greater "host resistance" than in adults. However, the cure of 6 out of 15 clinic patients, together with other observations of one of us (English, unpublished evidence), shows that mild curable infections also occur among adults. Their precise incidence is unknown, as no general survey of the adult population has been undertaken.

The more persistent type of *T. mentagrophytes* infection, such as occurred in 9 out of 15 of the clinic patients, usually involved the sides and soles of the feet, and even the toenails, rather than simply the interdigital spaces. The occurrence of three such cases among the 22 school children shows that this type of infection does occur in children, but comparatively rarely. Taking the population as a whole, it seems likely that the easily resolved type of *T. mentagrophytes* infection is commoner than the more persistent variety.

There is much evidence that, whatever the reasons, tinea pedis is not a highly infectious disease (Marples and di Menna, 1949; Vanbreuseghem *et al.*, 1952; English, 1957; Gentles and Holmes, 1957). This being so, there would be little risk to other members of a family from a single case of a quickly resolved *T. mentagrophytes* infection, but the regular presence of a small percentage of such cases in a community (as occurs in boys' day schools in Bristol) could be a real danger during communal sports and swimming. On the other hand, a single persistent infection, often shedding larger quantities of inoculum from more extensively infected areas, would be very likely to infect other members of a family eventually; but such cases, certainly among children and possibly among adults, are uncommon enough to be of less importance in a community.

In reporting the results of the school survey (English and Gibson, 1959a) we noted a discrepancy between the proportions of *T. mentagrophytes* and *T. rubrum* infections found in the schools and in the dermatological clinics. That this is not attributable to any special resistance of youth to *T. rubrum* is shown by the approximately equal incidence of the two fungi in the children of clinic families, and confirmed by the observations of Scheffler (1958) on German school children. It is explained by the fact that very few *T. rubrum* infections are easily resolved and many progress to involve the toenails and even the hands. A far higher proportion of them than of *T. mentagrophytes* infections, therefore, eventually arrive at skin clinics.

Summary

The epidemiology of tinea pedis due to *Trichophyton mentagrophytes* (*interdigitale* type) has been studied in the families of 22 day-school children and 19 skin-clinic patients known to have suffered from the infection. The disease had spread to one contact in each of three of the school children's families (4%) and to 12 contacts in eight of the clinic patients' families (23%).

It was shown that the number of baths taken per week, and hence the risk of cross-infection in the family, rises with the social class of the subject. As clinic patients' families were generally drawn from higher social strata than those of the school children, this might offer a partial explanation for the high cross-infection rate in the former group.

Nineteen of the school children and 6 out of 15 of those clinic patients who had finished treatment had been cured of their infection when their families were examined. It is suggested that the high cure rate in the school children may also, in part, account for the low cross-infection rate in their families, and that easily resolved and persistent types of infection may be of somewhat different epidemiological importance in families and in communities.

The results are compared with those obtained in a previous survey of *T. rubrum* infections in the families of clinic patients.

We are grateful to the families for their co-operation. We are indebted to Dr. R. P. Warin and Dr. C. D. Evans, Bristol, and Dr. Catherine J. MacLaren, Weston-super-Mare, for permission to visit their patients; and to Dr. G. A. J. Ayliffe, Bristol, and Dr. J. C. Gentles, Glasgow, for criticism and suggestions.

REFERENCES

English, Mary P. (1957). *Brit. med. J.*, **1**, 744.
—— and Gibson, Mary D. (1959a). Ibid., **1**, 1442.
—— —— (1959b). Ibid., **1**, 1446.
—— and La Touche, C. J. (1957). *Brit. J. Derm.*, **69**, 311.
Gentles, J. C., and Holmes, J. G. (1957). *Brit. J. industr. Med.*, **14**, 22.
Ingram, J. T., and La Touche, C. J. (1957). *Brit. med. J.*, **1**, 886.
Marples, Mary J., and di Menna, Margaret E. (1949). *Med. J. Aust.*, **2**, 156.
Rothman, S., and Windhorst, D. (1957). *A.M.A. Arch. Derm.*, **75**, 270.
Scheffler, von H. S. F. (1958). *Mykosen*, **1**, 102.
Sulzberger, M. B., and Baer, R. L. (1955). *Yearbook of Dermatology and Syphilology, 1954–5*, p. 10. Chicago.
Vanbreuseghem, R., Peeters, P., and Tritsmans, E. (1952). *Arch. belges Derm.*, **8**, 343.

In *The Church's Ministry of Healing* the Rev. A. H. Purcell Fox describes the nature of the healing ministry in Christian teaching, and discusses the various ways in which it can be exercised according to the forms prescribed by the Church. (Longmans, Green and Co. Ltd.; 115+xiv pp.; 10s. 6d.)

SHORT-LEG SYNDROME*

BY

P. J. R. NICHOLS, D.M., D.Phys.Med.

Specialist in Physical Medicine, Royal Air Force

There is no general agreement on the incidence of different leg lengths in otherwise normal subjects, or on how much this difference may be associated with symptoms. The recorded incidence of difference in leg length will depend on the method of assessment and the selection of subjects. The smaller the unit of measurement the greater will be the incidence, and the larger the unit of measurement the greater will be the agreement between observers.

Clinically Significant Degree of Difference in Leg Lengths

The amount of this difference associated with symptoms has been variously assessed: ¼ in. (6 mm.) (Butler, 1946; Stoddard, 1954); ⅓ in. (8 mm.) (Wiles, 1949); ½ in. (12.5 mm.) (Redler, 1952); ⅝ in. (21 mm.) (Barr, Stinchfield, and Reidy, 1950). The recorded incidence of differences of ¼ in. (6 mm.) or more is three to four times that of differences of ½ in. (12.5 mm.), both in controls and in patients with low backache (Rush and Steiner, 1946; Stoddard, 1954).

The clinically significant difference in leg length can be established by comparison of the incidence of various differences in leg lengths in patients with symptoms and controls. To do this the results of four published series are compared (Table I).

TABLE I.—*Incidence of Differences in Leg Length*

Series	Recorded Difference in Leg Length	No. of Subjects	Incidence %
Normal Subjects			
Ronstrom (1953)	1 mm.	67	95
Rush and Steiner (1946)	1 mm.	100	71
Ronstrom (1953)	6 mm.	67	67
Rush and Steiner (1946)	6 mm.	100	33
Stoddard (1954)	¼ in. (6 mm.)	50	28
Rush and Steiner (1946)	11 mm.	100	4
Stoddard (1954)	½ in. (12·5 mm.)	50	8
Allan (1953)	½ in. (12·5 mm.)	?	4
Patients with Low Backache			
Rush and Steiner (1946)	1 mm.	1,000	77
" " "	6 mm.	1,000	38
Stoddard (1954)	¼ in. (6 mm.)	100	60
Rush and Steiner (1946)	11 mm.	1,000	15
Stoddard (1954)	½ in. (12·5 mm.)	100	17

The largest and most carefully studied series was that of Rush and Steiner (1946). Though they did not carry out any analyses, it can be demonstrated from their results that only differences of 11 mm. or more are statistically significant in relation to clinical symptoms. Application of the χ^2 test revealed that a significant difference in the incidence of "short leg" in soldiers with backache and in control subjects can be demonstrated only when the degree of short leg is 11 mm. or more.

Accuracy of Clinical Measurements of Differences in Leg Lengths

Clinical observations are notoriously inaccurate. Schilling, Hughes, and Dingwall-Fordyce (1955) found that two observers disagreed by ½ in. (12.5 mm.) or more in 42% of occasions when measuring chest expansion. Though clinical measurements of leg lengths are subject to error (assessed by Dunlap and Kooda (1949) as ¼ in. —6 mm.) low backache is such a common problem that a simple clinical method of assessment of differences in length is desirable.

An experiment was therefore carried out to assess these differences by measuring the distance from the anterior superior iliac spines to the tip of the medial malleoli for each leg in the supine patient. Differences were recorded to the nearest ¼ in., the lower reading being taken in the case of intermediate values.

Statistical analysis of the result of this investigation (Nichols and Bailey, 1955) led to the conclusion that the overall degree of accuracy in the measurement of leg length is such that differences of ½ in. or more may be accepted as diagnostically significant. Differences of less than ½ in. are not reliable unless based on the average of at least four independent measurements. Their investigation also established individual accuracy and led to the acceptance of a recorded difference in leg length of ½ in. or more as the criterion for the clinical diagnosis of short leg.

An investigation was then carried out to answer the following questions: (1) What is the incidence of the clinical deformity of short leg? (2) Is there a significant difference between the incidence of short leg in the general population and in patients with low backache? The investigation was made at a Royal Air Force rehabilitation unit. The leg lengths of all admissions were recorded for a year. This gave 180 cases of "orthopaedic low backache" for comparison with 1,007 patients who gave no history of backache and who had suffered no injury or disability which could have altered the length of one or both of their legs.

Results of the Investigation

A recorded difference of ½ in. or more in their leg lengths was found in 7% (72 patients) of the control series and in 22% (39 patients) of the low-backache series (Table II). These results show close agreement with other published series (see Table III), the variations being within the limits of experimental error in the normals and due to selection in the backache series, yet the other two series were based on complicated costly radiological techniques.

TABLE II.—*Observed Incidence of Short Leg (Short Leg is Defined as a Difference in Leg Length of ½ in. (12.5 mm.) or More, Assessed Clinically)*

	Total	Short Leg
Control Series		
Medical cases	93	8 (9%)
Surgical "	40	3 (8%)
Neurological cases	38	3 (8%)
Orthopaedic cases (other than backache)	836	58 (7%)
Total	1,007	72 (7%)
Low-backache Series		
Postural defects	69	7 (10%)
Congenital "	21	2 (10%)
Prolapsed intervertebral disk lesions	74	23 (31%)
Short-leg syndrome	7	7
Undiagnosed	9	—
Total	180	39 (22%)

Diagnosis

The clinical diagnosis of short leg is defined as depending on the presence of a difference in leg length of ½ in.

*This paper is based on material for a thesis accepted by Oxford University for the degree of D.M.

TABLE III.—*Comparison of Series—Incidence of Leg-length Differences of ½ in. or More or 11 mm. or More (Incidence Expressed as Percentage of Total Cases)*

Series	Total Cases	Incidence of Short Leg
Controls		
Rush and Steiner (1946)	100	4
Stoddard (1954)	50	8
Present series	1,007	7
Low Backache		
Rush and Steiner (1946)	1,000	15
Stoddard (1954)	100	17
Present series	180	22

or more. The clinical diagnosis of short-leg syndrome assumes the presence of short leg with associated symptoms.

During this investigation seven patients were seen whose low backache was found to be primarily due to a short leg, and who responded to correction of the deformity by raising the height of the shoe. Subsequently, further cases of short-leg syndrome have been seen. The patients were all in-patients for at least four weeks and were followed up at three-monthly intervals.

Seventeen cases diagnosed as short-leg syndrome have been collected. The physical findings were similar in all of them. One leg was ½ in. or more shorter than the other. On the side of the short leg the shoulder was held lower, the hip was less prominent, and there was a loss of the hollow of the flank. The gluteal fold on the side of the short leg was lower than on the other buttock. There was a compensatory scoliosis and tilt of the pelvis (Fig. 1). Straight-leg raising was full in 13 of the patients and 70 degrees or more in the remaining four.

FIG. 1.—Short left leg. Left hip less prominent. Loss of hollow of left flank. Left gluteal fold lower than right. Plumbline falls from midline towards the left ankle.

Full clinical examination failed to reveal any definitive signs of other conditions which might explain the patients' symptoms. The erythrocyte sedimentation rate was normal, and radiological examination of the pelvis and lumbar spine failed to reveal any organic lesion. They were all treated with general mobilizing and postural exercises.

The following case history is typical.

Case 1.—A 21-year-old airman began to complain of low backache soon after he joined the R.A.F. When first seen, six months after the onset of symptoms, all the movements of the spine were full and free. The straight-leg raising was full on both sides. The pelvis was tilted to the left, and he had a scoliosis which was fully correctable. The left leg was ½ in. shorter than the right. One week after fitting a ⅜-in. (9.5-mm.) shoe-raise his walking had improved and he had no low backache. Nineteen months after discharge he was still wearing a ⅜-in. shoe-raise and was still symptom-free.

Short Leg After Injury

Limp

One of the main problems encountered in rehabilitation after fractures of the lower limb is the establishment of a limp-free walk (Nichols and Parish, 1959). It has been our practice to correct any shortening at the earliest opportunity, as post-traumatic short leg has been found to be a potent cause of a persistent limp.

Case 2.—A 21-year-old armament mechanic sustained a comminuted fracture of the right tibia and fibula which was immobilized in plaster-of-Paris for 14 weeks. Two weeks after removal of the plaster he was admitted for rehabilitation. When first seen he walked with a pronounced limp. The knee range was 180–135 degrees on the side of the fracture. The right-ankle movements were almost full. The right leg was ½ in. shorter than the left owing to the fracture. After three weeks' rehabilitation his progress was not as good as expected. The ½-in. shortening of the right leg was then corrected by a ⅜-in. (9.5-mm.) shoe-raise, and his walking rapidly improved. Four weeks after fitting the shoe-raise he returned to full duty, with a full range of knee and ankle-movements, and without a limp.

Backache

Post-traumatic short leg may also give rise to low backache.

Case 3.—A 19-year-old soldier fractured the shaft of the right femur and was treated with a Thomas splint and skin traction. Four months after the fracture he was fitted with a calliper and discharged from hospital to his home. He attended the hospital physiotherapy department for mobilization of the knee and ankle. Six months after the injury he discarded the calliper, and after walking without support for a week or two he began for the first time in his life to get a dull low lumbar backache. The backache was precipitated by standing and walking. Nine months after the injury he was admitted to the rehabilitation unit as his functional recovery was slow. On examination the fracture was soundly united with slight angulation. The right leg was weak compared with the left, and there was some limitation of movements of the knee. The right leg was ½ in. shorter than the left. After two weeks' concentrated rehabilitation for the leg, with no change in the backache, he was given a ⅜-in. (9.5 mm.) shoe-raise. Within two days the backache was improving, and one week later he was completely symptom-free. He remained symptom-free during the final stages of rehabilitation, including long walks, running, and games—activity comparable with his normal training.

Delayed Symptomatology

Symptoms due to post-traumatic short leg may be delayed for many years.

Case 4.—An officer had sustained a fractured femur resulting in 1½ in. (38 mm.) of shortening at the age of 20 (Fig. 2). When he was 42 he began to get low back pain. This pain became increasingly frequent and severe, and interfered with his work. When first seen he was 49 years old. *X*-ray examination showed osteoarthritic changes of both hip-joints, and a shoe-raise was fitted to the right shoe. The shoe-raise was tapered from ¾ in. (19 mm.) at the heel to ⅜ in. (9.5 mm.) under the sole. There was an immediate response to the shoe-raise. Walking and standing became much less of a physical and psychological strain, and the backache was partially relieved. The low backache was not completely relieved until one month after the fitting of the shoe-raise, when a lumbo-sacral support was fitted. Two years later he was promoted and was having fewer symptoms than at any time during the previous nine years, though his duties were more arduous. Most of his symptoms could have been prevented by the fitting of a shoe-raise many years previously.

Delayed correction of post-traumatic short leg is, however, not always so successful.

Case 5.—A 48-year-old man was admitted with a three-months history of aching in and around the left ankle after activity. He had had a comminuted fracture of the left tibia and fibula at the age of 35. The left leg was 1¼ in. (32 mm.) shorter than the right, a difference due to the fracture. He had a scoliosis which was partially correctable, and all movements of the spine were slightly limited. General mobilizing exercise for the spine and ankle were supplemented by physiotherapy for the ankle, and a ⅛-in. (9.5-mm.) shoe-raise was fitted to the left shoe. The shoe-raise made him feel "more natural" and improved his walking. After wearing the shoe-raise for a few days he began to get a dull low backache which radiated to the left hip. The pain disappeared immediately the shoe-raise was removed.

FIG. 2.—Case 4. 1¼-in. (3.8-cm.) shortening of right leg. Photograph shows the feet in the "normal standing" position.

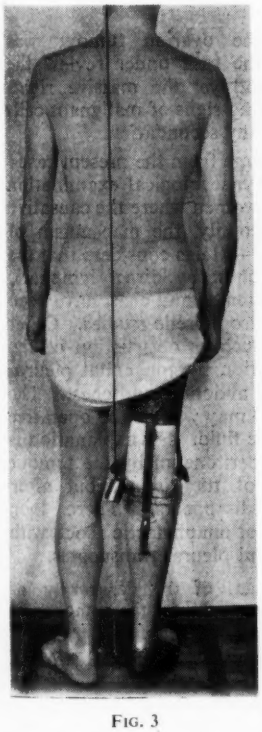


FIG. 3

FIG. 4

FIG. 3.—Case 6. Photograph showing the lateral tilt due to shortness of the right below-knee prosthesis; deviation indicated by plumbline falling from the left side of the neck to the midline between the knees. FIG. 4.—Case 6. Lateral tilt corrected by a shoe-raise of ½ in. (12.5 mm.).

D

"Artificial" Short Leg

The last case history illustrates an attack of low backache associated with a short artificial leg.

Case 6.—When first seen this 35-year-old officer had had a below-knee amputation of his right leg two years previously for severe injuries from an aircraft accident. The artificial limb which he had been wearing for several months felt a little short, but apart from a tendency to a "rolling" gait this did not inconvenience him. About two weeks after heavy activity involving lifting motor-car batteries he developed low backache. The pain steadily increased and was most severe when walking. Within a few days the pain was so severe that he had to discard his artificial limb and use crutches. Each time he attempted to walk with his prosthesis the backache became much worse again. He then fitted a temporary shoe-raise of about ½ in. to the artificial limb. Within two days he was able to walk pain-free. He had no other treatment of any kind. Wearing this new prosthesis, he had remained symptom-free for six months (Figs. 3 and 4).

Conclusions

Asymptomatic idiopathic short leg occurs in approximately 7% of the population without giving rise to symptoms.

Short leg may be associated with low backache, or with pains in the leg (short-leg syndrome). The backache is usually gradual in onset, starting in late adolescence or early adult life; it may be precipitated by the additional strains of military service or by a minor injury, particularly a strain caused by lifting.

Short leg due to injury may delay the expected recovery during rehabilitation of leg fractures; or, if uncorrected, may precipitate degenerative changes in the weight-bearing joints in later life. Post-traumatic short leg may also give rise to low backache.

Short leg occurring coincidently with other disabilities, which may themselves give rise to low backache, may act as an aggravating factor, but in many cases it is unrelated to the symptoms. There appears to be no way of assessing the part played by short leg other than a trial of a shoe-raise.

The treatment of short leg is by an appropriate shoe-raise. Response to treatment is usually good, but appears to depend partly on the patient's age and the mobility of the lumbar spine. The diagnosis and treatment of differences in leg lengths may prevent much inconvenience and suffering.

I thank the Director-General Medical Services, Royal Air Force, for permission to publish this paper, and Air Commodore L. McK. Crooks, Consultant in Orthopaedic Surgery to the Royal Air Force, for his help and encouragement.

REFERENCES

Allan, J. C. (1953). *S. Afr. J. med. Sci.*, **18**, 105.
Barr, J. S., Stinchfield, A. J., and Reidy, J. A. (1950). *J. Bone Jt Surg.*, **32A**, 793.
Butler, J. M. (1946). *J.-Lancet*, **66**, 10.
Dunlap, K., and Kooda, J. C. (1949). *Milit. Surg.*, **106**, 373.
Nichols, P. J. R., and Bailey, N. T. J. (1955). *Brit. med. J.*, **2**, 1247.
—— and Parish, J. G. (1959). *Ann. phys. Med.*, **5**, 73.
Redler, I. (1952). *New Orleans med. Surg. J.*, **104**, 308.
Ronstrom, G. N. (1953). *J. Louisiana med. Soc.*, **105**, 476.
Rush, W. A., and Steiner, H. A. (1946). *Amer. J. Roentgenol.*, **56**, 616.
Schilling, R. S. F., Hughes, J. P. W., and Dingwall-Fordyce, I. (1955). *Brit. med. J.*, **1**, 65.
Stoddard, A. (1954). In *Proceedings of the International Congress of Physical Medicine, London, 1952*, p. 260.
Wiles, P. (1949). *Essentials of Orthopaedics*. Churchill, London.

Medical Memoranda

A Case of Meigs's Syndrome

The following case is reported because of the relative rarity of the condition. The presenting symptom was breathlessness, the immediate finding was gross right-sided pleural effusion, and the cause of the trouble was a right-sided ovarian carcinoma. The essential features of Meigs's (1934) syndrome are hydrothorax and ascites, associated with disease of the ovary. The patients are relieved of their serous fluids by removal of the tumour.

CASE REPORT

On February 7, 1958, I was consulted by a woman aged 41, the mother of two children, who found it difficult even to walk; she had to be supported by two relatives. She looked extremely ill. Marked dyspnoea was at once obvious and the ankles were slightly oedematous, giving the immediate picture of cardio-respiratory distress. The chief complaints were breathlessness, swelling of the ankles, weakness, and tiredness, and she added that she had recently been passing less urine than usual. These symptoms had been noticed over the past half-year but had become distressing during the previous month. She had suffered from asthma at intervals for 10 years, but gave no history of any other illness. Her menstrual cycle was normal and there was no intermenstrual bleeding or discharge.

On examination there was pallor of the skin and conjunctivae, but no cyanosis. The veins of the neck were slightly engorged, but no abnormality was detected in the jugular venous pulse. The temperature was 98.2° F. (36.8° C.) and pulse rate 84. There was slight pitting oedema of the ankles. The apex beat was diffuse in the sixth space and outside the mid-clavicular line; the heart sounds, however, were normal; there were no murmurs audible and the blood-pressure was 126/72.

Examination of the respiratory system revealed a large right-sided pleural effusion extending to the level of the third rib, with absolute dullness and absence of air entry. There was slight dullness in both flanks, and she appeared to be tender low down in the right iliac fossa. This last finding, together with the right-sided pleural effusion, suggested the possible diagnosis of Meigs's syndrome, and she was admitted to hospital for further investigation.

On February 8 investigations showed: haemoglobin, 10.36 g./100 ml.; W.B.C., 6,800/c.mm.; E.S.R., 18 mm. (Westergren). The urine contained no albumin or sugar. A chest radiograph on February 11 showed a large right pleural effusion with the heart displaced and rotated to the left; and on the same day 100 ml. of straw-coloured fluid was aspirated from the right chest for cytological examination. On February 15 500 ml. was also aspirated. Examination of the fluid aspirated on the eleventh was reported on as follows: "The fluid contains blood and is highly cellular, but most of the cells are identifiable as pleural mesothelial cells. There are no malignant cells."

Further radiographs on February 17 and 20 still showed a large hydropneumothorax to the level of the first interspace.

The patient was transferred to a gynaecological hospital. At operation on February 21 2 pints (1,140 ml.) of straw-coloured fluid was removed from the peritoneal cavity and 5 ml. of similar fluid was aspirated from the right pleural cavity. A right-sided ovarian cyst the size of a large grapefruit and adhesions (orginally thought to be due to endometriosis, but possibly secondaries in view of the subsequent pathological report) stretching between the vaginal vault and rectum were found. A subtotal hysterectomy and bilateral salpingo-oophorectomy was performed. During the laparotomy the liver, gall-bladder, and stomach were felt to be normal.

The ovarian tumour measured approximately 9 cm. across. The greater part of it was solid, and was composed of friable greyish-white tumour tissue, but there were areas with a multilocular cystic structure. Microscopically the solid portions showed the structure of a papillary adenocarcinoma of the ovary, and the cystic areas that of a serous cystadenoma lined by hyperactive columnar epithelium. The uterus, tubes, left ovary, and appendix showed no gross or microscopical abnormality.

The patient made an uneventful recovery and was given a course of deep *x*-ray therapy to the pelvis in view of the possible residual secondary involvement. In mid-March she was allowed to return home feeling very fit and well, and up to January, 1960, no further fluid has been found in the pleural or peritoneal cavities.

X-ray examination of the chest on April 12 was reported on as follows: "Lung markings are slightly heavy, more in the bases. There are some thickened markings in the right apex due to scarring. There is a slight pleural thickening in the right lower segment, but no fluid can be detected nor are there any signs of pulmonary secondaries."

COMMENT

Lawson Tait (1892) operated on a woman aged 36 who had had repeated paracentesis of the chest and abdomen. During the previous year some 400 quarts (455 litres) of thin clear yellowish fluid had been removed from the chest and abdomen. At operation an ovarian fibroma weighing 2 lb. 2 oz. (965 g.) was removed. The outcome is described as having been successful. By 1943 Meigs *et al.* had discovered 30 cases of the same syndrome, and Beaumont (1950) has described another.

In all of these cases the ovarian tumour was fibromatous in origin. In the case under review the tumour was a carcinoma and yet the massive right-sided pleural effusion showed no signs of malignant cells nor did the *x*-ray film show any secondaries.

Two factors of interest emerge from the present case: firstly, the importance of a gynaecological examination in cases of pleural effusion in women where the causative factor is in doubt; and, secondly, the mechanism of the hydrothorax in such cases—Meigs considers that the fluid probably reaches the chest by direct lymphatic drainage: the fluids in the abdomen and chest have been shown to be identical by electrophoretic studies. Other views have been suggested, such as obstruction of the azygos vein, and communication by congenital pleuro-peritoneal canals between the abdomen and chest. The alarm reaction of Selye (1936) may well be the operative factor in the production of the fluid. His explanation is that repeated trauma to the peritoneum by the tumour first provokes a resistance of the tissues, but after some time the resistance disappears. There then appears a histamine toxicosis or anaphylactic shock with accumulation of peritoneal and pleural transudates.

I thank Dr. Shanmugaratnam, of the department of pathology, General Hospital, Singapore, for the pathological report.

E. LAIDLAW THOMSON, M.D., F.R.C.P.Ed.,
Singapore.

REFERENCES

Beaumont, G. E. (1950). *Applied Medicine*, p. 168. Churchill, London.
Meigs, J. V. (1934). *Tumors of the Female Pelvic Organs*, p. 262. Macmillan, New York.
—— Armstrong, S. H., and Hamilton, H. H. (1943). *Amer. J. Obstet. Gynec.*, **46**, 19.
Selye, H. (1936). *Nature (Lond.)*, **138**, 32.
Tait, L. (1892). *Med.-chir. Trans.*, **75**, 109.

Reviews

RHEUMATIC FEVER

Rheumatic Fever. Epidemiology and Prevention. Proceedings of a Seminar held at the International Children's Centre, Paris, September 25–27, 1956. Edited by R. Cruickshank, M.D., Ch.B., F.R.C.P., D.P.H., and A. A. Glynn, M.B., B.S., M.R.C.P. (Pp. 193; illustrated. 25s.) Oxford: Blackwell Scientific Publications. 1959

This monograph on the epidemiology and prevention of rheumatic fever contains the papers presented by a group of experts at the International Children's Centre, Paris, in September, 1956. The inclusion of the comments of members of the audience on the main papers is perhaps superfluous, but in no way detracts from the intrinsic value of the monograph as a whole.

The clinician is almost certain to find himself in deep water in the technicalities of the papers devoted to bacteriology and the antigen–antibody studies which have in recent years illuminated the streptococcal scene. From these specialized studies he cannot fail to draw comfort from the fact that the clinical inferences of Poynton's pioneer work in 1913 are now substantiated by abundant definite and separate approaches to the problem. The evidence for the indictment of the group A, β-haemolytic streptococci is conclusive, and as such provides an intelligible basis for the understanding of rheumatic fever whether it appears in sporadic or in epidemic form. In parenthesis it may be questioned whether rheumatic fever as such can be considered truly epidemic, however little doubt there can be that the number of cases increases in streptococcal epidemics.

Streptococcal epidemics in closed communities may develop *per se*, but are most violent when associated with a concomitant coryzal infection; and the incidence of complications, of which rheumatic fever can be regarded as only one, is determined not only by the infecting streptococcal seed but by the human soil on which it falls. Streptococcal disease in an individual is a "personal" affair, and its manifestations when it plays upon a community in epidemic form are determined by the idiosyncrasies and susceptibilities of individuals.

However successful may be the therapeutic and prophylactic measures adopted to control the dissemination of streptococcal infections there still remain a number of clinical features as yet unexplained, such as the relative immunity from rheumatic fever of children in the first five years of life, the absence of any reliable means for predicting or detecting potentially rheumatic individuals, and the pronounced tendency of the disease to smoulder in a relatively symptomless way and then to flare into a relapse with any subsequent streptococcal infection. It is reasonable to suppose that some host factor or factors, as yet unidentified, must be of fundamental importance.

Why is it that all children do not get rheumatic fever following their, on average, biennial attack of streptococcal sore throat? Socio-medical factors such as poverty, malnutrition, and overcrowding, with the inevitable repeated exposure of susceptible individuals to infected carriers, are demonstrably important even in those countries with high living-standards. However important these known and unknown factors may prove to be, from the practical point of view they are insignificant beside the known basic factor of Group A β-haemolytic streptococcal infection.

Two features of outstanding importance in this connexion have been demonstrated beyond question or doubt. First, that though the prompt and complete elimination of an acute streptococcal infection with one of the many effective drugs available is important in any individual patient, it is of over-riding importance in a patient known to have had rheumatic fever. Secondly, that relapses can be prevented by creating favourable environmental conditions and, more specifically, by using drugs both to control streptococcal epidemics and to protect susceptible individuals by long-term therapy.

That such measures can effectively protect individuals has been conclusively proved by controlled studies, though the best way of achieving this protection has yet to be decided. It is doubtful whether oral sulphonamides or long-acting antibiotics are the answer because of the uncertainty of absorption and because the maintenance of an effective level in the blood is so completely dependent upon that unpredictable factor the patient. This vitally important objective can most surely be attained by administering a parenteral antibiotic such as benzathine penicillin.

There can be no doubt that this monograph will be of the greatest interest to all clinicians, epidemiologists, bacteriologists, and public health administrators and will be provocative of ideas for future research.

F. G. HOBSON.

BLINDNESS IN AFRICA

Blindness in West Africa. By F. C. Rodger, M.D., Ch.M., D.O.M.S. Foreword by Sir Stewart Duke-Elder, G.C.V.O., D.Sc., LL.D., M.D., F.R.C.S. (Pp. 262+xiv; illustrated. 70s.) London: H. K. Lewis and Co., Ltd., for Royal Commonwealth Society for the Blind. 1959.

There are some 200,000,000 people in Africa. All but a small number live under primitive conditions which vary enormously over the different parts of the continent. Adequate statistics concerning the blind are available for the white population of South Africa; for the rest, information is scanty. In general terms it is clear that there is an immense amount of blindness arising from neglect, which itself reflects both the lack of medical facilities and the low standards of living. Over the whole of the continent there is much uncontrolled infection, some of which is known to produce ocular complications and some suspected of doing so. The wide range of nutritional habits and the gross malnutrition prevalent in Africa are yet further causes of ocular disabilities. How little is known of all this is apparent from the fact that even now textbooks state that the negro has a racial immunity to trachoma, whilst onchocerciasis, which is held to be responsible for blinding and uprooting whole communities, is of relatively recent recognition. A clear picture of blindness in Africa is likely to emerge only after many prolonged and painstaking studies, and it is likely that such studies will clarify many nutritional problems in ophthalmology and perhaps also problems of infection.

Humanitarian as well as scientific considerations therefore justify the considerable attention given of late by the Royal Commonwealth Society for the Blind to blindness in Commonwealth Africa. The Society were fortunate in obtaining the services of Dr. F. C. Rodger, who spent the better part of five years from 1952 on a field study in West Africa. The various papers he has published have given statistical and pathological information on the causes of blindness and on the role of onchocerciasis. This work has helped to lay the basis for concrete measures in treatment. The present volume is essentially a recapitulation of these studies, and it is good to have them in permanent form. How

far we are from any final assessment of the points at issue is clear from the fact that, though in the present volume onchocerciasis ranks high amongst the causes of blindness, recent work by other observers has questioned whether onchocerciasis is a blinding affection at all; it is said that much that goes as onchocerciasis must be regarded as unrecognized genetic disorders in the African population. A welcome beginning has, however, been made.

ARNOLD SORSBY.

KINETICS OF CELL GROWTH

The Kinetics of Cellular Proliferation. Edited by Frederick Stohlman, Jr., M.D. (Pp. 456+xiv; illustrated. $5.75.) New York, London: Grune and Stratton. 1959.

Kinetics is that branch of mechanics that treats of the action of forces in producing or changing the motion of bodies. In this particular symposium not only the action of forces on the motion of cells is considered but also their growth rate, their rate of liberation from the sites of their production and growth, and the factors which govern these. The methods familiar to most of us are discussed in some detail and contrasted with the exciting, more dynamic inventions that now occupy much of the time of the younger haematologists. Special place is devoted to studies with DNA labels, especially tritium-labelled thymidine, from which we are learning a good deal about cell turnover in blood and blood-forming tissues as well as DNA synthesis. Many of the results are, of course, so recent that it is difficult to assess their value. Obviously they must be chewed over, criticized, and modified before they become part of the everyday make-up of the clinician.

The reviewer gained much help and pleasure from the articles on the production and life-span of platelets (p. 278), the kinetics of red-cell proliferation (p. 318), and the excellent summaries of the new erythropoietic-stimulating factor that already rejoices in a variety of names (pp. 332–59). A friendly squabble by two British investigators over the fate of lymphocytes adds a certain piquancy to the proceedings. Dr. Eugene P. Cronkite deserves a special pat on the back for his sharp reminder of the glorious past of haematology (p. 445). The reader with more than average knowledge of higher mathematics will find plenty to intrigue him in the remarks on changing populations and steady-state kinetics.

This is a book that must be browsed through by all who take a serious interest in the blood. The articles and discussions are most efficiently assembled, charts and illustrations are clear, and the index is reliable.

ROY CAMERON.

AGE AND THE SPINAL CORD

The Effect of Advancing Age upon the Human Spinal Cord. By L. Raymond Morrison, M.D., with the collaboration of Stanley Cobb, M.D., and Walter Bauer, M.D. (Pp. 127+x; illustrated. 48s.) Cambridge, Mass: Harvard University Press. London: Oxford University Press. 1959.

This is a posthumous work of a descriptive character which neuropathologists will find clear, useful, and informative, especially those who work in geriatric units. The object of the study was to establish a baseline or normal control for any studies of the ageing human spinal cord. A series of "run-of-the-mill" spinal cords was studied as they came to necropsy at a general hospital from patients who had shown during life no neurological symptoms. Thirty-one cords were examined ranging from the second to the ninth decades inclusive. The principal histological changes met with in advancing age comprised, first, a generalized increase in the thickness of the meninges. Calcification was found only twice, however. A variable degree of myelin loss was met with, especially in the posterior columns but to a lesser degree in the lateral columns also. This change was visible in two-thirds of the cases, and it seemed clear that factors other than age were responsible for the alterations in the myelin. There was a correlation between degeneration of the posterior root fibres and changes in the posterior column. Several types of change were encountered in the anterior horn cells, particularly pigmentary atrophy, whereby the lipo-fuchsin increases at the expense of the Nissl substance. Shrinkage of cells was less common than one might have expected. For technical reasons cell counts were not attempted. Replacement gliosis, which was part of a grey matter gliosis, was often observed. Where perivascular demyelination occurs local proliferations of macroglia were seen. Arteriosclerosis of the spinal cord proved to be a relatively rare condition. Alzheimer cells and senile plaques were found in no instance.

MACDONALD CRITCHLEY.

DETOXICATION MECHANISMS

Detoxication Mechanisms. The Metabolism and Detoxication of Drugs, Toxic Substances, and Other Organic Compounds. By R. Tecwyn Williams, Ph.D.(Wales), D.Sc. (Birmingham). Second edition. (Pp. 796+x. £6 6s.) London: Chapman and Hall, Ltd. 1959.

Since the first edition of *Detoxication Mechanisms*, by Dr. R. Tecwyn Williams, was published in 1947, knowledge of the mechanisms of conjugation and enzymatic processes within the body has vastly increased, and in this edition many new problems are discussed and elucidated. The twenty years between 1875 and 1895 were most fruitful in uncovering the process called "detoxication," though Dr. Williams is careful to explain that not all conversions of foreign substances in the body result in the formation of toxic substances. Nevertheless, the toxic properties of many organic compounds and even the carcinogenic action of some are largely dependent on their metabolic fate, and the correlation of the differences in toxicity of members of the same group with their different metabolites provides a valuable confirmatory contribution to what has hitherto been only suspected or suggested. One of the outstanding examples of this correlation is the lower toxicity of xylene and toluene, which are converted mainly to the non-toxic benzoic and hippuric acids, compared with that of benzene, which forms phenol derivatives.

One of the most interesting features of the book is its emphasis on the part played by the bodily enzymes on the conjugation processes. Substances which have a marked inhibitory effect on enzymes are usually highly toxic. Organic phosphorus compounds inhibit cholesterinase; the free cyanide ion formed during metabolism of the nitriles reacts, under the influence of the enzyme rhodinase, present especially in the liver, with thiosulphate, with a detoxicating effect; mescaline produces its hallucinatory effect not by virtue of its metabolite but probably by the inhibition of a "mescaline oxidase" which animals resistant to its action are said to possess.

These are only a few examples of the immense variety of foreign organic compounds described; these range from industrial solvents, metallic poisons, insecticides, and drugs to colouring matter in food and drink. The author admits that it is difficult to decide to what extent a

systematic true detoxication occurs in the body and how far it is completely efficient, but his close examination, with a very extensive bibliography, of all the different reactions has certainly increased the knowledge of these problems and elucidated many of them. This is a book which will appeal primarily to the biochemist, but industrial physicians, clinicians, and physiologists will also find it an invaluable source of reference when faced with the problem of the toxic action of any substance foreign to the human body.

ETHEL BROWNING.

ALMOST ALL ABOUT SURGEONS

The Triumph of Surgery. By Jürgen Thorwald. (Pp. 483. 25s.) London: Thames and Hudson. 1960.

Dr. Jürgen Thorwald is a deservedly successful writer. It is stated that 350,000 copies of his last book *The Century of the Surgeon* were sold, and *The Triumph of Surgery* is likely to sell equally well, for it is clearly written and translated into excellent idiomatic English.

The plan of the author is the same in both books. He chooses some definite advance in surgery, reads up all about it in every available original source, and brings in a certain Dr. Hartmann to tell the story. Though the incredible journeys of Dr. Hartmann from continent to continent and his hobnobbing with the leading surgeons in various countries sometimes irritate the reader, there is no doubt that the stories are effectively told.

In this volume are related accounts of the early discoveries in cerebral localization, the first removal of a cerebral tumour (by Godlee), Kocher's establishment of thyroid surgery, Horsley's first operation for tumour of the spinal cord, the story of the pioneers of gall-bladder surgery, Bassini's work on hernia, and a full account of the development of local and regional analgesia. The final section deals with the contributions of J. B. Murphy and Sauerbruch to early thoracic surgery and ends with a description of the original efforts at transplantation of the cornea. As an interlude there is inserted an account of the tragic illness of the German Crown Prince, afterwards the Emperor Friedrich III.

The dates and essential facts are accurate—I only noted three factual errors in the whole book—but the author too often makes drama out of the ordinary and converts what is genuinely dramatic into melodrama. The references are extensive, but English readers will be surprised that two of Stephen Paget's contributions are attributed to his father, and they will scarcely recognize "Bland, Sulton" as the name of the author of *The Story of a Surgeon*, while "Critchley" without the "Macdonald" looks rather lonely.

ZACHARY COPE.

The *British Pharmaceutical Codex* is an indispensable companion volume to the *British Pharmacopoeia*. It is published by the Pharmaceutical Society, whereas the *B.P.* is published by the General Medical Council. While the *B.P.* is concerned with setting out standards for the preparation of drugs, the *B.P.C.* not only does this for many drugs not included in the *B.P.* but includes also much useful information of a pharmaceutical and pharmacological character. It does not give the contents of proprietary preparations; for that information the reader must turn to *The Extra Pharmacopoeia*, better known as "Martindale," also published by the Pharmaceutical Society. The 1959 edition of the *B.P.C.* (pp. xxix+1,301; 70s.) contains 70 new monographs, and the material throughout has been thoroughly revised since the previous edition appeared in 1954.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received.

Treatise on Parapsychology: Essay on the Scientific Interpretation of the Human Phenomena known as 'Supernatural.' By René Sudre. Translated by C. E. Green. (Pp. 412. 35s.) London: George Allen and Unwin, Ltd. 1960.

The British Journal Photographic Almanac 1960. Edited by Arthur J. Dalladay, A.Inst.P., F.I.B.P., F.R.P.S. (Pp. 620; illustrated. 8s. (board covers); 10s. (cloth bound).) London: Henry Greenwood and Co., Ltd. 1960.

Run Softly Demerara. By Zahra Freeth. (Pp. 220; illustrated. 21s.) London: George Allen and Unwin, Ltd. 1960.

The Integrity of the Personality. By Anthony Storr, M.B., B.Ch., M.R.C.P., D.P.M. (Pp. 174+ix. 15s.) London: William Heinemann Medical Books, Ltd. 1960.

Accidents and Ill-health at Work. By John L. Williams, LL.B. (Lond.). (Pp. 516. 45s.) London: Staples Press. 1960.

International Work in Leprosy, 1948-1959. (Pp. 39; illustrated. 1s. 9d.) Geneva: World Health Organization. London: H.M. Stationery Office. 1960.

Pathology of Infancy and Childhood. By Agnes R. Macgregor, M.D., F.R.C.P.Ed., F.R.C.O.G. (Pp. 631+viii; illustrated. 75s.) Edinburgh and London: E. and S. Livingstone, Ltd. 1960.

Der Diabetes Mellitus als Volkskrankheit und Seine Beziehung zur Ernährung. By Professor Dr. Ernst-Günther Schenck and Professor Dr. C. H. Mellinghoff. (Pp. 310+xi; illustrated. DM. 54.) Darmstadt: Dr. Dietrich Steinkopff Verlag. 1960.

Modern Scientific Aspects of Neurology. Edited by John N. Cumings, M.D., F.R.C.P. (Pp. 360; illustrated. 65s.) London: Edward Arnold (Publishers) Ltd. 1960.

Le Malattie del Fegato e delle Vie Biliari. By Giorgio Dominici. 2 Volumes. Third edition. (Pp. Vol. I: 1-1,128+xxvi; Vol. II: 1,129-1,942+xvi; illustrated. Vol. I: L. 16,500; Vol. II: L. 11,500.) Milan: Casa Editrice Dr. Francesco Vallardi. 1960.

Fluid Balance in Obstetrics. A Critical Review. By Philip Rhodes, M.A., M.B., F.R.C.S.(Eng.), M.R.C.O.G. (Pp. 169+x. 25s.) London: Lloyd-Luke (Medical Books) Ltd. 1960.

A Synopsis of Fevers and their Treatment. Revised by James H. Lawson, M.D.(Glas.), D.P.M. Tenth edition. (Pp. 184+viii. 10s.) London: Lloyd-Luke (Medical Books) Ltd. 1960.

Radiology as a Diagnostic Aid in Clinical Surgery. By Howard Middlemiss, M.D., F.F.R., D.M.R.D. (Pp. 151+viii; illustrated. 30s.) London: William Heinemann (Medical Books) Ltd. 1960.

Cerebral Dominance and its Relation to Psychological Function. By O. L. Zangwill, M.A. (Pp. 31+vii; illustrated. 10s. 6d.) Edinburgh and London: Oliver and Boyd for the William Ramsay Henderson Trust. 1960.

What Women Want to Know. A Noted Gynaecologist's Guide to the Personal Problems of Women's Health. By Harold M. Imerman, A.B., M.D., and T. Blanchard Dewey. (Pp. 224; illustrated. 18s.) London: Hammond, Hammond. 1960.

Dr. Kelly of Hopkins. Surgeon, Scientist, Christian. By Audrey W. Davis. (Pp. 242+xiv; illustrated. 40s.) Baltimore: Johns Hopkins Press. London: Oxford University Press. 1960.

Medische Ethiek en Gedragsleer. Third edition. (Pp. 299.) Amsterdam: Koninklijke Nederlandsche Maatschappij Tot Bevordering der Geneeskunst. 1960.

Achievement. Some Contributions of Animal Experiment to the Conquest of Disease. By Geoffrey Lapage, M.A., M.D., M.Sc. (Pp. 255+viii. 18s.) Cambridge: W. Heffer and Sons, Ltd. 1960.

Les Pancréatites Chroniques de l'Adulte. By H. Sarles and M. Mercadier, with the assistance of J.-Cl. Sarles, R. Muratore, and Cl. Guien. (Pp. 265; illustrated. NF. 36.) Paris: L'Expansion Scientifique Française. 1960.

Le Phénomène de Raynaud. Aspects Cliniques, Étio-pathogéniques et Thérapeutiques. By P. Langeron and L. Croccel. (Pp. 198+ix; illustrated. NF. 19.50.) Paris: L'Expansion Scientifique Française. 1960.

Fractions Coagulantes Préparées a Partir du Plasma Humain. Travail du Centre National de Transfusion Sanguine. Directed by J.-P. Soulier. (Pp. 2,440-2,599; illustrated.) Paris: Pathologie-Biologie. 1960.

BRITISH MEDICAL JOURNAL
LONDON
SATURDAY JUNE 18 1960

THE CRADLE OF NEUROLOGY

Unlike many of our British institutions which command respect by their hallowed traditions, the hospital which celebrates its centenary next week is, despite its hundred years of existence, as modern as a building by Le Corbusier. When the National Hospital was opened in a single house in Queen Square none of its supporters, even the most optimistic, could have foreseen its future as anything but another small and useful Victorian charity. Yet these homely surroundings were to be the scene of the growth and establishment of neurology as one of the more exacting of medical disciplines, of a medical and surgical advance against a group of disorders which had always been severely intractable to treatment. Those fortunate enough to attend the celebrations next week will hear members of the staff of the hospital and other eminent speakers reviewing the hospital's history and expounding the science of neurology to-day.

As Dr. Macdonald Critchley reminds us, in his elegantly written history of the hospital published in the *Journal* this week, it owed its origin to the compassion aroused by the apparently hopeless plight of the paralysed and epileptic, for whose medical care there were few or none who would accept responsibility. It would not have been surprising if the new hospital had set out only to supply the means for their decent care and management. From the first, however, cases presented for admission were carefully screened and a selection made of those for whom there was some hope of improvement. This important decision, misunderstood by some at the time as an attempt to escape responsibility for the most troublesome patients, was one inspired by courage and determination to achieve the apparently impossible and to restore to some measure of health and usefulness patients whom others had written off as a total liability. It was this decision which created the challenging atmosphere so necessary for research and discovery and the conditions which enabled an unusually gifted medical and surgical staff to lay the foundations of modern neurology.

The National Hospital has been called "the cradle of neurology," but we might expand the metaphor and call it the nursery and even the class-room for those wishing to learn the elements, and more, of this most intricate of the clinical sciences. When the National first opened its doors neurology was unknown as a specialty, despite Marshall Hall and Romberg. Specialism itself was indeed in its earliest stages, and the idea of a special hospital was generally disliked by the profession. The fact that during the first fifty years of the hospital's existence its honorary staff also held appointments in general hospitals removed many of the grounds for this dislike, and also ensured that the new knowledge which sprang from work carried out at the National Hospital should be spread as fast and as widely as possible. The measure of its success is that no large general hospital to-day is complete without its own department of neurology, staffed mainly by those who have received at least part of their training in Queen Square.

The hospital owes its world-wide reputation to the outstanding distinction of its staff, which has included Hughlings Jackson, the philosopher of neurology; Ferrier, the pioneer in neuropathology and experimental research on the central nervous system; Gowers, the dynamic leader of clinical neurology; and Victor Horsley, whom Harvey Cushing acclaimed as "the true pioneer in the surgery of the nervous system." Both Jackson and Ferrier were powerfully influenced by the teaching of the Edinburgh professor, Thomas Laycock, whose ideas would to-day be considered wildly speculative; and we may wonder how the careers of these giants of neurology would have developed if the National Hospital had not existed to provide a clinical laboratory where theories could be tested by observation and experiment. These men were all in advance of their time, and it has taken two or three generations to exploit their work fully. Only in the last generation have the possibilities of brain surgery come to be widely recognized. But by 1887 Horsley had already carried out 10 operations on the brain, and in 1890 he published an article in this journal[1] in which he included in "the various conditions of the brain and spinal cord which it is at the present time considered reasonable and justifiable to attack by surgical interference" depressed fractures; extradural, subdural, and intracerebral haematomas; hydrocephalus; and focal epilepsy, as well as brain tumours. Out of 44 cases of operation on the brain which he reported there were only 10 deaths, an astonishing achievement for the time. It was no wonder then that the stature of these men was acknowledged wherever the central nervous system and its disorders were studied. The out-patient department at Queen Square became the Mecca of neurologists from all over the world. The

[1] Horsley, V., *Brit. med. J.*, 1890, **2**, 1286.

penetrating clinical lectures given by Gowers, and the brilliant surgical demonstrations to be seen at the hospital, were to prove the significant turning-point in the lives of many who were to become pioneers of neurology in their own countries.

Following the characteristic pattern of many other institutions in this country, the National Hospital won its fame as a poor and struggling private enterprise, dependent upon charity for its needs. Yet it inaugurated new developments in hospital management by establishing the "day-room" for patients, by installing the first department of physical medicine and electrotherapy, by its employment and regular training of male nurses, and by its acceptance of paying patients. Its medical school, which has attracted students from all countries, won its fame without recognition or support from either government or university. The new Institute of Neurology, opened in 1938, was received into the University of London only in 1950, two years after the tremendous financial burdens imposed by the ravages of war had been finally resolved by the absorption of the hospital into the National Health Service.

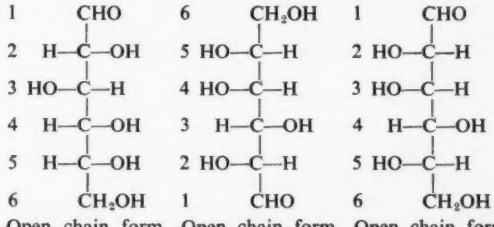
There can be few institutions anywhere with such a record of triumphant achievement in a single century. The cosy domestic interior of 1860 with its eight beds has grown into one of the great special hospitals of the world. In paying tribute to the talent and intellectual vigour—and even genius—which made possible this historical phenomenon we must remember, too, the indomitable spirit of Miss Johanna Chandler and the inexhaustible springs of compassion which nourished its early growth. And in the tradition of her act of *caritas* the Chartered Society of Queen Square, which is publishing a commemorative book on Queen Square next week, will devote any profits from it "to the social welfare of the paralysed and epileptic."

SYNTHESIS OF ASCORBIC ACID IN ANIMAL TISSUE

Ascorbic acid was first isolated over 30 years ago by Albert Szent-Györgyi, who obtained it from adrenal glands and from orange juice. At first the pure substance, named hexuronic acid by Szent-Györgyi, was not realized to be the hitherto elusive vitamin C, but recognition by Szent-Györgyi himself, quickly confirmed by others, led to the chemical synthesis of the vitamin, which was renamed L-ascorbic acid. The reason why many tissues of the animal body, including the adrenal glands, are rich in ascorbic acid is still not properly understood to-day.

Chemically ascorbic acid is the lactone of a sugar acid, a lactone being an internal anhydride formed by the removal of the elements of water between the carboxyl group of a hydroxy acid, and a hydroxy group of the acid. A full chemical description of ascorbic acid is: "the enolic form of 3-(or 2-) keto-L-gulonolactone"—that is, it is a lactone of an acid derived from the sugar L-gulose. L-Gulose is related to D-glucose in that if one replaces the $-CH_2OH$ group of D-glucose by an aldehyde group, and the aldehyde group of the open-chain form of glucose by a $-CH_2OH$ group, in effect interchanging the $-CH_2OH$ and $-CHO$ groups of the open-chain form of D-glucose, one obtains the open-chain form of L-gulose. The carbon atom one of D-glucose thus becomes carbon atom six of L-gulose.

Since by convention carbon atom one is written at the top of the straight chain formulae for sugars, the structure of D-glucose must be rotated through 180° in the plane of the paper in order to show its relationship to L-gulose. Thus:



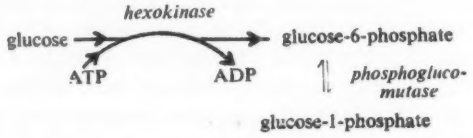
Open chain form of D-glucose (conventionally written formula) | Open chain form of D-glucose (unconventionally written formula) | Open chain form of L-gulose (conventionally written formula)

Most species of animal, guinea-pigs and primates being exceptions, can manufacture all that they need of ascorbic acid, whose importance cannot be doubted, and the means whereby plants and many animals synthesize this substance has been the subject of much study in recent years. In the rat, and in plant tissues, L-ascorbic acid can be formed from D-glucose by a series of reactions in which, as can be shown by experiments with radioactive sugars and by other means, the chain of six carbon atoms in the glucose molecule remains intact.[1-3] Moreover, as might be expected from the relationship between

[1] Jackel, S. S., Mosbach, E. H., Burns, J. J., and King, C. G., *J. biol. Chem.*, 1950, **186**, 569.
[2] Horwitz, H. H., Doerschuk, A. P., and King, C. G., ibid., 1952, **199**, 193.
[3] Isherwood, F. A., Chen, T. Y., and Mapson, L. W., *Biochem. J.*, 1954, **56**, 1.
[4] Burns, J. J., and Mosbach, E. H., *J. biol. Chem.*, 1956, **221**, 107.
[5] Hassan, M. ul, and Lehninger, A. L., ibid., 1956, **223**, 123.
[6] Burns, J. J., and Evans, C., ibid., 1956, **223**, 897.
[7] Chatterjee, I. B., Chatterjee, G. C., Ghosh, N. C., Ghosh, J. J., and Guha, B. C., *Biochem. J.*, 1960, **74**, 193.
[8] Mapson, L. W., Isherwood, F. A., and Chen, Y. T., ibid., 1954, **56**, 21.
[9] Loewus, F. A., Jang, R., and Seegmiller, C. G., *J. biol. Chem.*, 1956, **222**, 649.
[10] Mapson, L. W., and Breslow, E., *Biochem. J.*, 1958, **68**, 395.
[11] Touster, O., Hutcheson, R. M., and Rice, Louise, *J. biol. Chem.*, 1955, **215**, 677.
[12] Burns, J. J., Dayton, P. G., and Eisenberg, F., Jr., *Biochim. biophys. Acta*, 1957, **25**, 647.

D-glucose and L-gulose shown above, the rat converts [1-^{14}C] glucose to [6-^{14}C] ascorbic acid.[2 4]

The series of reactions involved in this interconversion is now largely understood. First, glucose is transformed into glucose-1-phosphate at the expense of the terminal phosphate group from adenosine triphosphate.



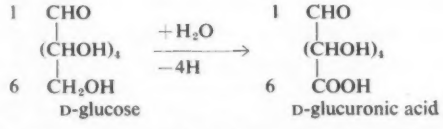
The glucose-1-phosphate can then react with uridine triphosphate to form uridine diphosphoglucose and pyrophosphate. Thus :

UTP + glucose-1-phosphate ⟶ UDP glucose + pyrophosphate

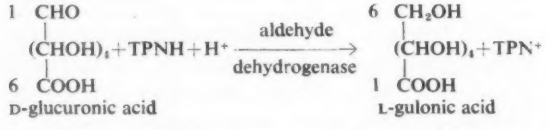
The glucose in the UDP glucose can then be oxidized to glucuronic acid: Thus

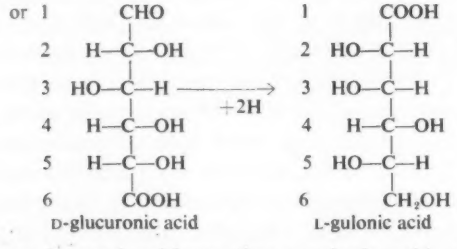
UDP-glucose + 2DPN$^+$ ⟶ UDP-glucuronic acid + 2DPNH + 2H$^+$

Hydrolysis of the UDP-glucuronic acid yields free glucuronic acid. The whole process can be summed up as:



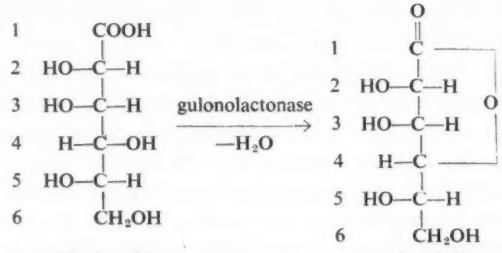
The D-glucuronic acid thus formed can be reduced to L-gulonic acid:





There is good evidence that L-gulonic acid, or its lactone, L-gulonolactone, can be converted to L-ascorbic acid in the rat.[5 6]

In the most recent of a series of papers on the biological synthesis of L-ascorbic acid, I. B. Chatterjee and colleagues[7] suggest that the conversion of L-gulonic acid into L-ascorbic acid involves first the formation of L-gulonolactone under the influence of an enzyme gulonolactonase. This enzyme is found in the soluble material when microsomes and other particles are spun down from a homogenate of liver tissue from the rat, goat, and guinea-pig, and of chick-kidney.



The formation of the lactone from the acid is a reversible process ; and, as might be expected of one which entails the liberation of water into the aqueous medium which pervades biological tissues, under biologically significant conditions the equilibrium favours the formation of the acid rather than that of the lactone. Chatterjee and colleagues suggest that the conversion of L-gulonic acid to L-gulonolactone may be the rate-limiting step in the biosynthetic chain.

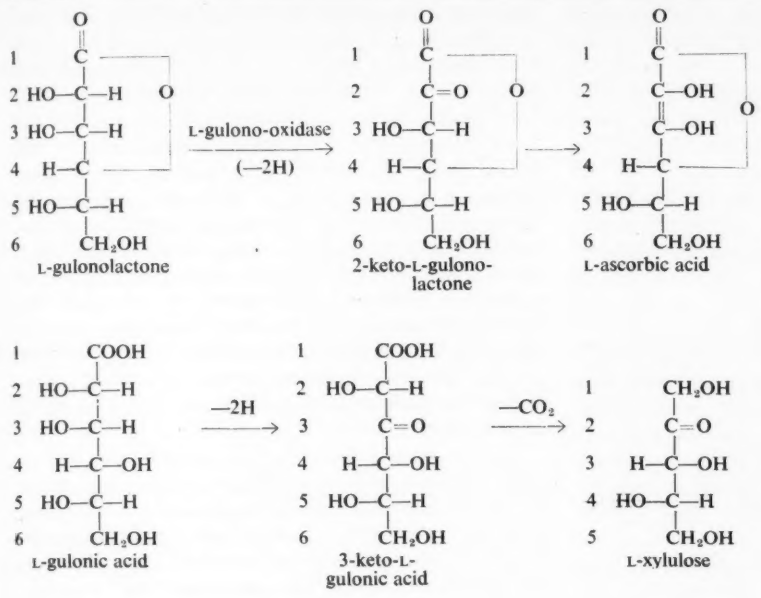
These workers have shown that an enzyme in the microsomes from rat and goat liver and from chick-kidney, L-gulono-oxidase, catalyses the oxidation of L-gulonolactone to 2-keto-L-gulonolactone. The latter can then spontaneously rearrange to give L-ascorbic acid (see upper formula opposite).

Although L-gulono-oxidase has not been obtained in a pure state, Chatterjee and colleagues have evidence that it may be a flavoprotein containing active –SH groups. This enzyme, interestingly enough, is absent from guinea-pig liver, and this absence probably accounts for the dependence of the guinea-pig upon a dietary source of ascorbic acid.

There is already experimental basis for the view that in plant tissues the biosynthesis of ascorbic acid can proceed from D-galactose, as well as from D-glucose, by an analogous series of reactions.[3 8-10]

D-galactose ⟶ D-galacturonic acid ⟶ L-galactonolactone ⟶ L-ascorbic acid.

It has been realized for some time that in animal tissues D-glucuronolactone[11] and L-gulonolactone[12] can both be converted to L-xylulose, a sugar excreted by human beings in abnormally large amounts in idiopathic pentosuria. Chatterjee and colleagues suggest[7] that the conversion of L-gulonic acid to L-xylulose differs from that involved in the transformation of L-gulonic acid to L-ascorbic acid in that, under the influence of the enzyme L-gulonic dehydrogenase, L-gulonic acid (the acid and not its lactone) can directly be oxidized to 3-keto-L-gulonic acid. The 3-keto-L-gulonic acid formed from L-gulonic acid



can be enzymically decarboxylated to yield L-xylulose (see lower formula above).

L-Xylulose is probably normally converted in the body to D-xylulose, which, after phosphorylation, can enter the glucose-monophosphate oxidative pathway.[12] In pentosuric subjects there is presumably a block in the process of conversion of L-xylulose to other intermediates, so that this sugar accumulates and is excreted.

If the processes in the human liver are similar to those in the liver of the guinea-pig, then men have died from scurvy in the past because their tissues lack L-gulono-oxidase. The fact that the metabolic gap which induces susceptibility to scurvy can be seen as part of a pattern of intermediary metabolism, in which another defect can lead to idiopathic pentosuria, is a fascinating example of the power of biochemical tools to lay bare the enzymic basis of health and disease.

A LOCAL HABITATION

Queen Square and the National Hospital 1860–1960[1] is an elegant and charming tribute to one of our national monuments. We learn that when the hospital wanted a matron in 1864 it advertised in *The Times* for "a well-educated Protestant Lady of evangelical principles, age from 30–45, to act in the above capacity," and that "no lady need apply whose character will not bear the strictest enquiry." When a German doctor, Dr. Pelman, visited Queen Square in 1869, he described the National as "a pure jewelcase," and observed that "the patients' rooms were furnished like the lounges of a first-class hotel. . . ." Photographs, prints, and maps give the reader a delightful and simple guide to Queen Square and its development. The anonymous author has collected a wealth of interesting detail about the square, its houses, and their inhabitants. At one time Elihu Yale lived there. William Morris moved to No. 26 in 1865, and for 17 years made it the centre of a factory for making tapestry, furniture, cloth, wallpapers, and illuminated manuscripts. The musician Dr. Charles Burney also lived in the square, and his famous daughter Fanny Burney.

The medical reader will turn eagerly to the pen portraits of great neurologists, and to the group photographs of the staffs of 1886 and 1906: what a collection of talent and genius! And it is a happy historical coincidence that the present chairman of the hospital, and writer of the foreword to this jewelcase of a book, is Sir Ernest Gowers.

[1] London: Edward Arnold (Publishers) Ltd. Price: 30s.

MULTIPLE ENDOCRINE ADENOMAS

Over the past 20 years there have been many reports of patients with multiple endocrine adenomas. The endocrine glands affected in this remarkable syndrome have been the pituitary, parathyroids, and pancreatic islets. Reviewing the literature up to 1953, L. C. Underdahl and colleagues[1] found 14 cases with proved adenomas of two or three of these glands. They also described eight new cases, in four of which the history suggested that there was a familial incidence. In 1954 P. Wermer[2] reported five members of a family with adenomas of one or more of these glands, multiple in three; and M. P. Moldawer and colleagues[3] described a father and daughter with multiple adenomas of the parathyroid glands. The father had also a pituitary tumour, and the daughter hyperinsulinism due to two islet-cell tumours. Experience has shown that patients with this syndrome are likely to have more than one adenoma of the pancreatic islet cells or parathyroid glands, which is important from the surgeon's point of view. Clinically, the syndrome may be overlooked because only one endocrine disorder may be manifest for many years, though other glands may harbour adenomas.

[1] Underdahl, L. O., Woolner, L. B., and Black, B. M., *J. clin. Endocr.*, 1953, **13**, 20.
[2] Wermer, P., *Amer. J. Med.*, 1954, **16**, 363.
[3] Moldawer, M. P., Nardi, G. L., and Raker, J. W., *Amer. J. med. Sci.*, 1954, **228**, 190.
[4] Cooke, W. T., *et al.*, *Gut*, 1960, **1**, 71.
[5] Wermer, P., *Ann. intern. Med.*, 1958, **49**, 1403.
[6] Zubrod, C. G., ibid., 1958, **49**, 1389.

An interesting and puzzling feature of the syndrome is the high incidence of associated disorders of the upper alimentary tract. They may be the presenting feature. First, peptic ulceration may be present, often associated with polypoid hypertrophy of the gastric rugae. When associated with a non-insulin-secreting adenoma of the pancreas, this is known as the Zollinger–Ellison syndrome. Secondly, pancreatitis and pancreatic lithiasis, and, thirdly, persistent watery diarrhoea may occur. W. T. Cooke and colleagues[4] have recently drawn attention to this facet of the syndrome in the first issue of the new journal *Gut*. They describe the case of a 40-year-old woman who died from a bleeding duodenal ulcer. Ten years earlier she had experienced an attack of severe epigastric pain, and for two years had suffered from diarrhoea and recurrent renal colic. Investigation disclosed a urinary infection, impaired glucose tolerance, and suspected calcification of the pancreas. The findings at necropsy included jejunitis, hypertrophied gastric rugae, lithiasis of the left kidney, and multiple adenomas of the pancreas, parathyroid, and pituitary glands. Though the serum levels of calcium, phosphorus, and phosphatase and the urinary excretion of calcium had been normal during life, the bones showed histological changes of hyperparathyroidism.

The aetiology of this bizarre syndrome is obscure. It can hardly be secondary to the effects of a pituitary tumour, for there are no known adenohypophysial hormones with trophic actions on the parathyroid glands or pancreatic islets. The most plausible hypothesis so far advanced, and one to which the familial cases lend support, is that there is a genetic fault, possibly the absence of some chemical agent responsible for the development of endocrine glands.[5,6] But this does not explain why the pituitary and parathyroid glands and pancreatic islets should be the only ones affected. The associated alimentary disturbances are even harder to explain. They cannot be ascribed to the effects of hyperinsulinism, for the islet-cell tumours in these cases do not usually secrete insulin. Elucidation of this problem might provide a useful clue to the aetiology of peptic ulceration.

TOO MUCH TOMATO JUICE

The colour of certain vegetables and fruits is caused by the presence of long-chained, unsaturated hydrocarbons known as carotenoid pigments. Only one of these, β-carotene, is at all familiar medically—as the precursor of vitamin A. Carotinaemia is occasionally produced by the excessive consumption of carrots, and may be associated with diseases such as diabetes, hypothyroidism, nephrosis, and the lipoidoses, in which there is an increase in lipoproteins. An isomer of β-carotene, lycopene, is responsible for the red colour of tomatoes, as well as being present in many other vegetables, but it is only recently that the first case of lycopenaemia has been reported.[1] The patient was an elderly housewife with gastro-intestinal symptoms, who had been in the habit of consuming 2 litres of tomato juice every day for several years. She was found to have an orange-yellow pigmentation, most marked on the horny surfaces of the hands and feet and in the mucous membrane of the mouth. The distribution was similar to that seen in cases of carotinaemia, and, as in the latter, the sclerae and urine were unaffected, thus serving to distinguish the condition from jaundice. Carotenoid levels in the serum were very high, and spectrophotometry showed excessive peaks of carotene and lycopene, with absorption curves similar to those of the patient's favourite brand of tomato juice.

The patient was found to have gallstones as well as some impairment of liver function, and during the course of cholecystectomy a biopsy specimen was taken from the enlarged liver, which had a strange orange-yellow colour. Histological studies revealed collections of vacuoles scattered throughout the liver and fine yellow granules in the parenchymal cells, both of which stained with lipid stains and gave a fluorescence in ultra-violet light characteristic of lipochromes. Unlike β-carotene, lycopene probably has no metabolic role in man, and it is assumed that the deposits in the liver were degradation products. There was minimal histological evidence of liver damage, and it was thought unlikely that the lycopenaemia was responsible for any of the patient's symptoms. After operation she continued to have vague complaints, attributed by a psychiatrist to a mild depressive state. The case history bears a striking resemblance to that of patients with carotinaemia,[2] who are frequently obese, middle-aged females with nervous traits and an addiction to carrots.

SLUDGED RED CELLS

Sludging of the blood is of considerable interest because it is one of the few intravascular phenomena which can be observed directly in man and because of its possible relationship to thrombosis. We are indebted to the careful work of M. H. Knisely and associates for most of our knowledge of the subject.

An intravascular agglutination of the red cells which causes a disturbance in the flow pattern of blood in small vessels is thought to be the cause of the observed changes.[1] It has been said to be an *in vivo* equivalent of the erythrocyte sedimentation rate, J. S. Hirschbroek and M. Woo[2] finding an 80% correlation between sludging and sedimentation rate in over 600 cases. Knisely and colleagues[3] did not agree with this view and considered the adhesion of the red cells in sludging to be different from rouleaux formation (which is thought to be a much looser aggregation) occurring with

[1] Reich, P., Schwachman, H., and Craig, J. M., *New Engl. J. Med.*, 1960, **262**, 263.
[2] McConaghey, R. M. S., *Lancet*, 1952, **2**, 714.

sedimentation *in vitro*. Sludging has been studied in man by microscopical observation of the conjunctival vessels.[4] The individual red cells are not usually visible at the magnifications used, but the rate of flow of the columns of red cells and breaking up of the columns are visible. Considerable experience is required to interpret the appearances, and even then it is largely subjective.

Gross degrees of sludging are usually present in severely ill patients but rarely in entirely healthy people.[5] It has been observed in acute and chronic infections, trauma, malaria, allergic states, after acute cardiac infarction,[6] and in some cases of diabetes mellitus.[7 8] It has been reported in normal pregnancy and in most cases of pregnancy associated with disease.[9] High-fat meals may produce sludging in patients who have suffered from cardiac ischaemia[10] and also in the golden hamster.[11]

The significance of sludging is not known for certain, but it seems clear that, if the red cells are firmly enough stuck together, the fluidity of the blood may be seriously jeopardized, with consequent impairment of supply of oxygen to the tissues and possible predisposition to thrombosis. Red-cell agglutination may have a dominant role in causing the cellular conglomerates found in the capillaries of the liver and kidney in eclampsia.[12] Thus prevention or reversal of sludging might be important.

Heparin and dicoumarol[13] do not prevent or reverse sludging. Antihistaminics reverse it in allergic states[14] and steroids in acquired auto-immune haemolytic anaemia.[15] Antimalarial drugs abolish sludging in malaria and possibly in trauma and rheumatoid arthritis.[16] B. P. Madows[17] has recently given hydroxychloroquine sulphate to 44 patients with coronary, cerebral, or peripheral vascular disease (including thrombophlebitis); he noted abolition of sludging in most of them, and striking clinical benefits in these cases and in a case of sickle-cell anaemia. These observations, while interesting, must be interpreted with caution, since they constitute preliminary findings with no controls. Moreover, in angina and intermittent claudication it is very difficult to assess therapeutic effects clinically. A treatment in which the physician is interested will tend to benefit the patient.

[1] Knisely, M. H., in *Blood Clotting*, Josiah Macy Jr. Conference, edited by Flynn, 1951, p. 11.
[2] Hirschbroek, J. S., and Woo, M., *Amer. J. med. Sci.*, 1950, **219**, 538.
[3] Knisely, M. H., Bloch, E. H., Brooks, F., and Warner, L., ibid., 1950, **219**, 249.
[4] —— and Warner, L., in *Thrombosis and Embolism*. Proceedings of the 1st International Conference, Basel 1954. Edited by Th. Koller and W. R. Merz, 1955, Switzerland, p. 378.
[5] —— —— Eliot, T. S., and Warner, L., *Science*, 1947, **106**, 431.
[6] Bloch, E. H., *Amer. J. med. Sci.*, 1955, **229**, 280.
[7] Ditzel, J., and Sagild, U., *New Engl. J. Med.*, 1954, **250**, 587.
[8] Ashton, N., *Lancet*, 1959, **2**, 625.
[9] Odell, L. D., Aragon, G. T., and Pottinger, R. E., *Amer. J. Obstet. Gynec.*, 1947, **54**, 596.
[10] Higginbotham, A. C., Williams, A. V., and Knisely, M. H., *Anat. Rec.*, 1955, **121**, 310.
[11] Swank, R. L., and Cullen, C. F., *Proc. Soc. exp. Biol. (N.Y.)*, 1953, **82**, 381.
[12] Fahraeus, R., *Physiol. Rev.*, 1929, **9**, 241.
[13] Laufman, H., Martin, W. B., and Tanturi, C. A., *Science*, 1948, **108**, 283.
[14] Timonen, S., and Zilliacus, H., *Acta med. scand.*, 1949, **135**, 292.
[15] Wasastjerna, C., Dameshek, W., and Komninos, Z. D., *J. Lab. clin. Med.*, 1954, **43**, 98.
[16] Harders, H., *Thromb. Diath. haemorrh. (Stuttg.)*, 1957, **1**, 482.
[17] Madows, B. P., *J. Amer. med. Ass.*, 1960, **172**, 1630.

BIRTHDAY HONOURS

As vice-chancellor of Birmingham University Professor R. S. Aitken has had the formidable task of guiding it through a period of rapid expansion, and the conferment of a knighthood will be widely welcomed for the recognition it gives to the great services he has rendered this still growing university. Professor Aitken was formerly vice-chancellor of Otago, where he had qualified in medicine, and in 1938–48 was regius professor of medicine at Aberdeen; he came to Birmingham in 1953. Dr. W. E. Chiesman receives a knighthood for his distinguished service as Treasury medical adviser since 1945. The medical problems abounding in the industrial sphere early attracted Dr. Chiesman's attention, and he was for some years adviser to I.C.I. before going to the Treasury. At present he is president of the Association of Industrial Medical Officers. The knighthood conferred on Dr. J. S. Richardson marks the services he has rendered as a physician to so many people in all walks of life, and for some time he has had the added responsibility of being personal physician to the Prime Minister. As a teacher of clinical medicine at St. Thomas's, Dr. Richardson has a host of friends in his former students, who will warmly welcome this distinction. Also honoured for the lustre he has shed on the practice of medicine is Mr. B. W. Rycroft, consultant ophthalmic surgeon to the corneoplastic unit at the Queen Victoria Hospital, East Grinstead. One of the world's leading authorities on corneal grafting, Mr. Rycroft has greatly contributed to the advancement of ophthalmology in many ways. The distinguished New Zealand surgeon, Mr. Douglas Robb, receives a knighthood, an honour that will cause special pleasure in the B.M.A., since Mr. Robb has been nominated as the Association's President-elect for 1961–2.

The K.C.M.G. conferred on Dr. A. M. W. Rae is in recognition of his work over many years in West Africa and, more lately, in the Colonial Office. The K.B.E. goes to Air Vice-Marshal C. A. Rumball, a distinguished clinician who is senior consultant at the R.A.F. Central Medical Establishment. Lady Herring, wife of Sir E. F. Herring, lieutenant-governor of Victoria, Australia, is made a D.B.E. in recognition of her work for social welfare and nursing in Victoria. Lady Herring qualified in medicine at Melbourne.

The C.B.E. conferred on Dr. Ian Grant as past-president of the College of General Practitioners will please his many friends in the B.M.A., who have happy memories of him as Chairman of the Representative Body and for many years as a member of Council.

We record with regret the death on June 11 at the age of 51 of Professor Alexander Kennedy, professor of psychological medicine in the University of Edinburgh. A memoir will be published next week.

Drug Treatment of Disease

DRUGS IN THE TREATMENT OF OLD PEOPLE

BY

MARJORY WARREN, C.B.E., M.R.C.S., L.R.C.P.

Consultant Physician, Geriatric Unit, West Middlesex Hospital, Isleworth, Middlesex

Experimental Prescribing

Drug therapy has changed considerably during this century, and now it is possible to treat with drugs much more extensively and *more accurately* when a precise diagnosis has been established and a careful choice of drugs has been made.

To-day much more research is being undertaken into the physiological action and pharmacological properties of new drugs, and the advantages of such research are obvious. There are some disadvantages, however, in the spate of new drugs (often expensively and attractively advertised) which flood the market, and which the average doctor has too little time to study in detail.

This applies particularly to drugs advertised for the use of "geriatric patients." The field of geriatric medicine has of recent years come more to the fore, and, unless due care is taken in the choice of drugs, many old patients with conditions which cannot be cured may be allowed or even encouraged to become a "profitable" group for experimental prescribing. The temptation to use new drugs in these cases is especially great when an elderly patient is suffering from a long-standing clinical condition for which there is no known cure.

In trying new drugs advertised as useful for "geriatric patients" some care should be exercised in finding out the precise use of these new preparations.

Ideally new drugs should be submitted to carefully controlled clinical tests, so that their advantages, if any, can be assessed and compared with the older drugs given for the same condition. Some thought should also be given to avoiding the use of an expensive proprietary drug if there is a cheaper and equally useful preparation in the *British National Formulary*. This is especially important when prescribing for long-term disease, which characterizes so many of the clinical conditions found in older patients.

In treating old people almost the whole range of medical conditions may be encountered, and it is indeed commoner to find that several conditions co-exist than that there is only one. It is therefore often necessary to prescribe for more than one disease at a time. Classical disease in the old usually responds well to orthodox therapy, but it is always advisable to treat early and actively because the multiplicity of pathological conditions and a lowered level of reserve often make delay dangerous and success less likely. This is particularly important when the untreated condition tends to immobilize the patient—as, for example, when an elderly patient with a cardiac failure becomes immobilized and later bedridden by his oedema. In such cases prompt treatment with digitalis or diuretics or both relieves the discomfort and avoids such sequelae.

Accurate Diagnosis

The commonest symptoms for which elderly patients seek relief and advice include: pain and discomfort; giddiness with falls; weakness; shortness of breath; cough; inability to sleep; frequency of micturition; constipation; impairment of vision or hearing or both.

The commonest conditions for which elderly patients are brought to a doctor include: unsteadiness in getting about, with falls; loss of independence; weakness; mental confusion; incontinence of urine; diarrhoea, which on examination is not infrequently found to be retention of faeces with overflow.

The commonest conditions found on clinical examination of elderly patients include: cardiovascular disorders; cerebrovascular accidents; Parkinson's disease; arthritis; anaemia; respiratory infection; urinary infection; diabetes; malignant disease; renal failure with uraemia; myxoedema; ulcerated legs.

A glance at these lists suggests the great need for an accurate diagnosis before drug therapy is started, if failures are to be avoided. It is rarely necessary to prescribe a cough mixture to an older person to-day, as the commonest causes of cough are: heart failure, when digitalis and diuretics will be more effective; and a chest infection, which usually responds well to the appropriate antibiotic. In using mercurial diuretics the frequency of renal failure in the old should be remembered.

Analgesics

Aches and pains and discomforts of one sort and another are frequent concomitants of old age, and so requests for analgesics and sedatives are frequent. Seldom can pain be relieved specifically; hence the drugs prescribed may be needed for long periods, during which time the patient may become resistant to the drug with resultant lessening of effect. For this reason the physician must prescribe in such a way that he can increase and vary the drugs as the condition progresses and so continue to keep the patient comfortable. Pain may result from many different conditions, including the following.

Malignant Disease

In the early stages aspirin, or aspirin, phenacetin, and codeine, or compound codeine tablets, 1 tablet to be taken when needed and the dose later increased to several times daily, will be sufficient. Later such tablets can be prescribed six-hourly or four-hourly and/or in increased numbers. All these tablets should be crushed and taken in water to avoid irritation of the gastric mucosa. Later still pethidine in small doses, 25 mg. p.r.n., can be given in combination with the simpler analgesics already described. Finally, the dose of pethidine can be increased gradually to 50 mg. to 75 mg., to 100 mg. when needed, to six-hourly, to four-hourly. At the same time more specific treatment should not be omitted.

An old man complaining of "lumbago" or pain in his back, especially if he has some urinary symptoms, should be suspected of a carcinoma of the prostate. If this condition is established it should be treated with oestrogens—the commonest and most popular being

stilboestrol. With this therapy little in the way of analgesics is required—but the patient should be warned of possible side-effects. Similarly in the female, pain from an inoperable carcinoma of the breast may be controlled, at least in part, by oestrogens, but such treatment may have to be stopped if uterine haemorrhage occurs. In other cases testosterone propionate, 100 mg. weekly, may be the preparation of choice, and this is especially good in cases with bony metastases.

With inoperable lesions of the alimentary tract the addition of tincture of belladonna, 10 minims (0.6 ml.) in a mixture three times a day often relieves the muscle spasm associated with the neoplasm and delays the need for more than simple analgesics.

In the early stages of malignant disease in old people, if the drug treatment is good, then it is rare that morphine will be needed to keep the patient comfortable.

Coronary Artery Disease

Although coronary artery disease in the elderly often occurs without the initial pain which characterizes the disease in younger persons, yet when it is diagnosed morphine gr. $\frac{1}{8}$ (8 mg.), which may be repeated later if pain or restlessness is present, and a slow intravenous injection of aminophylline 0.25 g. in 10 ml., should be given without delay. The advisability of giving anticoagulants in the old is debatable—but prompt treatment as above is very desirable.

Peripheral Vascular Disease

This condition is commonly found in elderly patients, and pain is often the presenting symptom. In addition to simple analgesics such as aspirin, A.P.C., codein. co., and paracetamol, one of the vasodilators should be tried, and, if tolerated, given in increasing doses. There has been a good deal of discussion about the usefulness of such drugs, yet from a practical point of view experience shows that not only do patients get relief of pain but also that improvement in the peripheral circulation occurs as demonstrated by the colour and temperature of the part affected (usually part of the lower limb).

It should be remembered that some patients experience uncomfortable side-effects described by them as a "sinking feeling," "fullness in the chest," and nausea. These are probably due to a stimulation of excessive gastric juice, and due care must be exercised in the use of such drugs in patients who may have a gastric ulcer.

The vasodilator of choice is probably tolazoline ("priscol"), and doses found useful are as follows: 25 mg. first day, 25 mg. b.d. for two days, 25 mg. t.d.s. for three days, 25 mg. q.i.d., 50 mg. b.d., etc., to a maximum dose in some cases of 100 mg. q.i.d.

Arthritis

The pain associated with arthritis includes that due to rheumatoid arthritis, to degenerative joint disease (osteoarthritis), and to a combination of both, and is one of the most difficult types to control. Pain can be persistent in spite of analgesics—indeed, overdoses of aspirin are not uncommonly found in patients who have still failed to overcome their pain. As described above, simple analgesics should be given in small doses, varied, and not more often than is needed. In spite of all such precautions, however, difficulties will still be experienced in controlling the pain. For rheumatoid arthritis corticosteroids may be given in short courses with very gratifying results.

Cramps

Old people often complain much of discomfort associated with "cramp," usually in the lower limbs. This may be due to cold, and if so can easily be remedied, but that due to pathological conditions is often difficult to control. Peripheral vascular disease is one cause, and this can be most effectively treated with tolazoline, as already described.

Cramp due to spasticity of muscle with irregular contractions, often found in patients with disseminated sclerosis, is very resistant to treatment, and trial and error with so-called "muscle relaxants" may be the only treatment possible.

In some patients clinical examination reveals no specific cause for the condition, and in these cases of unknown aetiology the cramp may be improved with large doses of vitamin B_1, 25 to 100 mg. t.d.s., and in addition quinine sulphate, 2 gr. (130 mg.) at night is worth a trial.

Osteoporosis

This is a common cause of backache in old people, and is best relieved by a combination of hormones, calcium, and diet.

Paget's Disease of Bone

This condition, which must be differentiated from osteoporosis, calls for no specific treatment. The intelligent and careful use of various analgesics in small doses gives the best results.

Sedatives

This group of drugs is more in danger of abuse than any other. Many of the conditions found among elderly patients lend themselves to such abuse, and equally are brought about by overdosage.

Sleeplessness

Old people living alone often sleep for short periods during the day; these in the aggregate may be many hours, but they do not satisfy the desire to sleep and interfere with unbroken sleep at night. On the whole, the old need less sleep than the young, and so, unless there is some very good reason to prescribe sedatives in such cases, it is wrong to do so.

Night sedation often results in night incontinence and tends to drowsiness by day and so indirectly to dehydration and uraemia, especially in patients who already have some renal failure.

In the writer's experience, too, many elderly patients who have slept well for many weeks in hospital without drugs fall a prey to night sedation as soon as they return home. Simple remedies, other than drugs, should always be given a trial first.

Sleeplessness with Mental Disturbance

There are times when a patient who becomes mentally confused at night and rather overstimulated may need sedation, and then the time for giving the drug and the dose are equally important. When the regular pattern of disturbance is known, it is wise to prepare the patient by giving an early dose of the drug of choice.

For example, if an old person is known to become restless and confused at 10 p.m., then it may be wise to give sedation earlier at 8 p.m. and repeat the dose once later. In spite of the enormous list of new drugs from which to choose, the value of many is still unproved, and, until fully controlled clinical tests have been undertaken, there is no great merit in using these newer, but

still experimental, preparations. Hence for many chlorpromazine hydrochloride ("largactil") seems, in spite of the known possible side-effects on the liver, to be a safe and reliable drug and the one of choice. Many slightly restless and confused patients settle well on a single dose of 25 mg. or 50 mg. given at bed-time, or given in a repeated dose 25 mg. + 25 mg. as already described.

Other reliable and safe drugs are chloral hydrate 20 gr. (1.3 g.), which in many cases is very effective, and paraldehyde. This latter, though very safe, should be avoided as often as possible, because the characteristic smell and taste linger and sometimes add to the patient's delusions that of poisoning.

In principle, too, barbiturates should be given only for short periods, as accumulation of these drugs tends to produce confusion. In some instances, however, the short-acting drugs have their uses for patients who are temporarily inclined to wander at night, especially when in unfamiliar surroundings. Minimum doses should always be tried first.

Sleeplessness with Pain

When pain is the cause of lack of sleep, it should be treated primarily and the patient receive minimal added sedation. It cannot be too frequently stated that the prescription of night sedation, without differentiation between the various factors responsible, must be regarded as *undertreatment*, and this applies equally at home and in hospital. With adequate personal care and attention drugs can be reduced to a minimum, with great advantage to the patient.

Tranquillizers

Tranquillizers are closely allied to sedatives, but usually have less hypnotic effect; they are aimed at relaxing tense and anxious psychoneurotic patients. These drugs are useful in treating elderly patients with early mental changes and are often effective in controlling behaviour, so that an old person can remain living in normal surroundings.

Before any pronouncement can be made on the choice of such drugs, more clinical tests must be undertaken.

Cardiac Conditions

For old people with gross cardiac failure and without renal failure, the most effective diuretic is mersalyl, 2 ml., given by intramuscular injection, which may be needed daily for some days initially; and later on once or twice weekly. In obstinate cases non-mercurial diuretics such as hydrochlorothiazide may be combined with mersalyl, and in mild cases hydrochlorothiazide may be given alone four or five days weekly. If an elderly patient is not reliable and diuretics are essential, it may be wiser to arrange for injections of mersalyl to be given.

Infections

The whole range of antibiotics are much used and are invaluable in the treatment of old people, especially for pulmonary and urinary infections. Whenever possible, sensitivity tests should be undertaken, so that the therapy is specific, as this gives better results and avoids waste. In treating pulmonary infections the use of aminophylline as a respiratory stimulant is often advisable.

Diabetes

This is a rather different disease in old people. In many instances it is mild, requiring attention to diet only, and the patient needs no drug therapy. In other cases the disease is difficult to control and calls for a careful watch on dosage of antidiabetic therapy.

If insulin is used, a dose should be determined so that one early-morning injection only is sufficient. This is especially important for old people, because few can give injections to themselves. The use of oral antidiabetic drugs has solved some of these problems, but if an old person is forgetful or is considered unreliable in taking them, then insulin by injection may be considered the preparation of choice.

Parkinson's Disease

Patients with Parkinsonian rigidity benefit from one of the antispasmodic drugs. The commonest drug used to-day is probably benzhexol ("artane," "pipanol"), which should be started in small doses, because of the tendency to mental confusion as a side-effect. The drug is supplied in 2-mg. and 5-mg. tablets, and should be prescribed conveniently so as to avoid the necessity of cutting the tablets. It is recommended than benzhexol should be given in very slowly increasing doses starting with 1 mg. (¼ tablet daily), to 2 mg. daily, to the same dose b.d., t.d.s., q.i.d., then 5 m.g. b.d., t.d.s., and so on until the optimum dose is determined. If the patient becomes, at any stage, mentally confused, the dose should be reduced, and the patient should *not* be sedated, as this may increase the confusion. Benzhexol is of no value in treating Parkinsonian tremor.

Blood Diseases

Routine blood examinations reveal a surprising number of macrocytic anaemias and even some leukaemias in addition to the commoner iron-deficiency anaemia. In all cases, therefore, when anaemia is suspected, a blood examination should be made, including film. Treatment with vitamin B_{12} and/or folic acid before an accurate diagnosis has been made may well spoil the chance of making a correct assessment later.

Anticoagulants

The use of anticoagulants in the treatment of elderly patients is a highly controversial subject and will not be discussed here. Suffice it to say that if or when anticoagulants are used, then the procedure is exactly as with other patients, though haemorrhage is a little more apt to occur in old and arteriosclerotic patients.

Ulcerated Legs

Treatments for ulceration of the legs are as numerous as the staff treating them; and probably equal success may be obtained by many and various methods. But whatever applications are used, there is a strong argument for firm supporting bandages—with at times pressure pads—and infrequent dressings—that is, weekly or fortnightly.

Other points worthy of consideration are (1) the presence of oedema, which retards healing and which should be treated at the same time, and (2) the so-called ulcer which is in fact an infected bleb caused by oedema, often part of a congestive cardiac failure. Such "ulcers" usually heal spontaneously if the cardiac failure is adequately treated.

Constipation

Many old people are inclined to develop a "bowel complex," and they should be advised not to worry

unduly if there is not a daily bowel action. When constipation is present (and the presenting symptom may be alleged diarrhoea due to retention of faeces with overflow), the regular use of roughage in the diet and sufficient fluid intake should not be overlooked in giving advice on the subject.

In choosing an aperient it is wise to consult the patient, as many know what suits them best and may be very sensitive to dosage.

In addition to senna, cascara, and saline aperients, which form a good basis for treatment, two other preparations may prove useful: (1) methyl cellulose, which acts by increasing the bulk of the faeces and so stimulating peristalsis; and (2) dioctyl sodium sulphosuccinate ("dioctyl-medo"), a drug which acts by penetrating and making the faeces flocculent—a useful treatment for impacted faeces.

In combination with aperients or as an alternative many elderly patients favour the use of suppositories. Enemata should not normally be needed except for an emergency and for patients who are permanently incontinent of faeces.

Anorexia

This may be due to many conditions, physical or psychological or both, and is often associated with loss of morale or even with the presence of mild depression. Morale is essential to good health in elderly patients, and diet normally plays an important part in maintaining a sense of well-being.

Consequently, when there is loss of appetite, all factors likely to be responsible should be considered, and prescribing bitters or tonics to improve the appetite may be found appropriate.

Conclusion

In treating old people the following principles must be remembered:

1. Drug therapy should be as "streamlined" as possible, limited to the fewest drugs and ordered in the simplest way.

2. Treatment should be adequate and given with as little delay as possible.

3. Psychologically it is always better to avoid injections if oral preparations are satisfactory, as patients quickly become dependent upon the "prick."

4. The frailties of old people should be considered in the following ways and special precautions taken when prescribing for them:

(*a*) Be sure that an elderly patient has heard and understood instructions.

(*b*) Warn the patient of possible side-effects, and advise him what to do if these occur.

(*c*) Be sure that eyesight is good enough to read the directions.

5. Ascertain that the patient is mentally reliable to take what has been prescribed, and that he understands the importance of doing so.

6. Arrange that he is able to reach the surgery or hospital when his drugs are finished, or alternatively that he has someone interested who will.

I wish to acknowledge my thanks to D. G. Wood, Chief Pharmacist, West Middlesex Hospital, for his help in reading through this paper.

E

A VISIT TO THE U.S.A.

BY

J. O. F. DAVIES, M.D., D.P.H.

Senior Administrative Medical Officer, Oxford Regional Hospital Board

The purpose of my visit to the U.S.A. was to study schemes of patient care and to note the developments in design and planning of hospitals. I spent over seven weeks in the U.S.A., and 10 days in Puerto Rico, where an interesting experiment in regionalization of hospitals is taking place. The visit was made possible by a grant from the Rockefeller Foundation.

Hospital Development

It is not generally realized that the population of the United States increased by 35m. over the years 1940–55. Three times as many persons were admitted to hospital in 1955 as were admitted in 1935. How have the hospitals kept up with such increased utilization?

Under the Hill Burton Programme the Federal Government has assisted in the building of between 3,000 and 4,000 new hospitals since the end of the war, providing over 135,000 beds; 1,200 projects which will add a further 52,000 beds are under construction, and others in the pre-construction stage will provide nearly another 11,000 beds. Financial assistance has been provided by means of a "matching contribution," which varies from one-third to two-thirds of the total cost of the hospital. The local sponsoring body may be public or private, but the hospital must be non-profit-making and provide a community service. The plans must reach certain minimum standards laid down by the United States Public Health Service, and to that end they are examined by officers of the department. This examination also provides opportunities for suggestions to be made to the sponsoring body, but every scope is given for local preference. The United States Public Health Department, as a general guide to hospital planning, has issued a large number of important publications in the form of "guide material" which covers every aspect of hospital planning and construction. They range from "A Prototype Study—600-bed hospital" through "The Hospital Laboratory—Equipment and Supply Lists," to "Recommended Lighting Practices," and are freely available and contain mines of information.

More than half the new hospitals have fewer than 50 beds, 20% have from 50 to 99 beds, and the remaining 22% have 100 beds or more. Half the projects are located in communities with a population under 5,000. Not all the new hospitals in the United States are provided under the Hill Burton Programme, however. Some of the most interesting examples of those which have been built privately are the 10 hospitals of the United Mineworkers in West Virginia and Kentucky, and the Permanente Hospitals of San Francisco and Los Angeles, originally provided in association with the Kaiser Foundation.

The deficit of beds in the United States hospitals is still thought to be great, and estimates suggest that about 850,000 more are required to meet the nation's peace-time needs. Though nearly 200,000 beds are now being provided under the Hill Burton Programme, progress in remedying this shortage is said to be slow because of

population increases and obsolescence of existing facilities. The standard to which the United States Public Health Department has worked so far as general beds are concerned is 4.5 per thousand of the population.

Hospital Staffing

It is, of course, difficult to generalize about hospitals in the United States, but in the voluntary non-profit-making hospitals, as opposed to state, municipal, veteran, or federal, the medical staffing differs considerably from that in this country. In addition to specialists on the staff of a hospital most of the general practitioners of the area also hold hospital appointments and are able to admit fee-paying patients under their care. A hospital of 300 beds may well have between 150 and 200 attached doctors. This large number of doctors results in the number of operating theatres in America being far in excess of those in this country. Many doctors undertake surgical lists which are much shorter than those seen in English hospitals, and may attend to operate on one case only.

The Health Information Foundation of New York, in a survey in 1955, ascertained that 52% of surgery in America was undertaken by general practitioners, not all of whom had passed the American Board specialty examinations. The American Joint Commission on the Accreditation of Hospitals is doing a great deal to stimulate the control of the standard of professional care by the medical staffs of hospitals by requiring the establishment of medical records committees, tissue committees (which comment critically on the justifiability or otherwise of surgical procedures undertaken), and credentials committees (which examine the qualifications of applicants to the hospital staff).

American non-teaching hospitals are experiencing increasing difficulty in staffing hospitals at "intern" and "resident" levels. There are 5,000 more approved internships than there are graduates to fill them. The hospitals that succeed in attracting residents provide married quarters and set themselves out to make available an adequate postgraduate training, even in some cases going to the length of appointing a whole-time director of medical education for this purpose. An interesting idea for the British observer is the "chief of service" system. In some hospitals one clinician in medicine and one in surgery is designated "chief of service." He is the medical administrator responsible for the whole of the medical or surgical side of the hospital and co-ordinates the efforts of the surgeons. It seems that he has a not unimportant part in determining the level of clinical care which the hospital provides.

Hospital Design

One of the features that has influenced ward design is the prepayment insurance schemes. These provide varying standards of benefit, resulting in almost universal provision of private or semi-private accommodation in single rooms or rooms where three or four, or at most six, patients share accommodation. These rooms may open off a single corridor centrally or off a double corridor (the race-track design). The size of the ward unit is usually about 30 beds, though in one of the United Mineworkers' Hospitals there were 70 beds to a floor, and in the Herbert Moffatt Hospital, San Francisco, there were 50 beds to a ward.

The use of air-conditioning allows more internal rooms than in this country. Generous provision of lavatories, even to single rooms, makes it possible to deal with men and women on the same nursing unit and makes for flexibility in admitting men or women according to demand. The space in the rectangle of the race-track is large, and includes a nursing station with clean and "dirty" utility rooms, and treatment rooms. There is nothing makeshift about some of these nursing stations, which are equipped with telephones, call systems, pneumatic-tube delivery service, and medicine- and chart-rooms. A room is provided in which doctors may dictate letters and interview patients and relatives. The nursing station is also the location of the ward clerk, who is in constant attendance during office hours. Nearly all the planned nursing units seen are devised with the idea of making the nurses' journeys shorter, so that they tend to be placed at the centre of the area served.

Another interesting ward pattern is the Y-shaped ward, with the service rooms in the stem of the Y, the wards being entered centrally.

Central Sterilization

No hospital is without its central sterilization and supply department. This means there is one central supply distributing agency in each hospital, responsible for providing the nurse and the doctor with their needs. While central sterilization departments vary in their lay-out, all undertake the preparation and sterilization of instruments, syringes, dressings, gowns, gloves, and sterile solutions. Sterilizing no longer takes place in the various departments of the hospital, and there is no sterilizing in the wards. The time of the nurse in the ward is thus saved. Some of the workers in central supply departments make up standard packs for every sterile procedure or operation carried out in the hospital. The packs are labelled so that the contents are clear to the user. They are wrapped in linen or paper, and have the merit of being sterile. The number of British hospitals which have in recent years shown that their sterilizing procedures do not result in the preparation of sterile dressings and utensils makes it clear that the central sterilizing department is much needed in this country.

An interesting feature observed in the United States is the increasing use of disposable equipment. Paper cloths, paper bags to line containers, and paper covers, even to the cover of the cotton sheet on the examination couch, changed with each patient, are widely in evidence. Wax carton medicine-cups and drinking-vessels and plastic enema sets are in general use. A number of hospitals are using disposable syringes and needles, though these are at the moment relatively expensive. Nevertheless, these hospitals still claim that on balance the savings on the use of disposable syringes make them an economic proposition.

One of the likely developments of central sterilization is the preparation of packs for standard procedures, not by the central supply department but by the manufacturer. The use of cobalt for sterilizing may make it possible for these packs to be provided sterile and ready for use. The central supply department to be developed in hospitals in this country may well as a consequence be much smaller than those seen in America, as it may be possible to introduce sterile or unsterile pre-packaged

goods at various stages of the central supply production line.

The materials provided for operating theatres generally come from the central supply department, but to some extent theatres in the United States have elected to remain outside the central supply system. There seems to be no good reason for this. There may, however, be a need for a small, very rapid sterilizer in operating theatres to deal with the occasional dropped instrument.

Operating Theatres

Most hospitals have a centralized operating department with a generous supply of rather smaller theatres than are seen in England. There are no separate anaesthetic rooms. Despite the fact that some operating theatres continue to look after their own sterilization, central supply of materials tends to allow the structure to be more compact. Nearly all the larger hospitals provide rooms adjoining the theatre in which patients remain until they have recovered from the anaesthetic.

Recovery Rooms and Intensive Nursing-care Units

Recovery rooms vary in size and in the duration of the patients' stay in hours. These post-operative units are highly equipped and well staffed. In some instances they have been expanded into what are called "intensive nursing-care units." This development appears to be the result of the shortage of trained nurses. Some intensive nursing care units admit any seriously ill patient, not necessarily after operation; and patients with active gastro-intestinal bleeding or severe burns, for example, may be admitted to these special care units. Another development on which there is much discussion is "progressive patient care." The objective is stated to be the tailoring of services to the individual nursing needs of the patient. Three grades of care are generally envisaged—intensive, intermediate, and minimum or self-care. Whilst a number of hospitals claim to be undertaking progressive care, few in fact appear to be doing so. Segregation of patients according to their nursing needs, instead of sex, age, and type of illness, whether medical or surgical, is an interesting experiment in making the maximum use of skilled nursing care, but it is doubtful whether the Americans themselves have yet come to any final conclusions on this experiment.

Catering

Throughout the United States meals for all staff are provided on the cafeteria system. In this way the number of catering staff is reduced to a minimum. The food is wide in variety, and is attractively prepared. The cafeteria is under the control of the catering department, as is the service of meals to the wards. An interesting method of serving meals to the wards is the "tray-veyor" system. A moving belt in the kitchen conveys the tray between two lines of personnel—one serving hot foods, the other serving cold. The trays are checked at the end of the conveyor belt with the menu card before passing into a lift which carries the food to a point near the nursing station of the ward concerned. The distribution and serving of the food is the concern of the catering staff, not the nursing staff. The food arrives at the patient's bedside quickly, and is according to the patient's choice, a menu having been shown to them beforehand. Another method is delivery of food in electrically heated containers, as in England. With the tray-veyor system the machinery is put into reverse at the end of the meal and the trays are automatically unloaded into the dish-washing machine in the kitchen.

Other Departments of the Hospital

X-ray departments of hospitals of any size are very well equipped. Automatic bulk-processing units are common in radiodiagnostic departments, and are said to economize in staff. On the radiotherapy side many hospitals possess modern equipment in the shape of cobalt units and linear accelerators. Laboratories are generous in size, and in many instances have provision for research. Equipment is plentiful, and benches and sinks are of a very high quality. Nearly all hospitals have emergency rooms or casualty departments. Many of these are supplied with beds so that anxious casualty officers are not confronted with the choice of sending a patient home or admitting him to a ward in the hospital. The patient can be watched under the control of the casualty officer for a period of hours or, if need be, days. This useful facility also avoids the disturbing effect of admitting a patient to a ward at night.

Out-patient departments in non-teaching hospitals are as a rule not comparable with those seen in this country. The nearest approach to the English out-patient department is that seen in the United Mineworkers' and the Permanente Hospitals. Many hospitals provide consulting rooms on a rental basis for consultants on the staff of the hospital. The clinician provides his own receptionist or nurse, and technical investigations are undertaken in the hospital *x*-ray departments or laboratories on a payment basis. In many instances the out-patient department is so constructed as to be suitable for private consulting practice.

Nursing

It was of great interest to find that the problems of nursing in the United States are very similar to those in England. There is a relative shortage of nurses, though the numbers of trained personnel per thousand of the population are higher than in England. The Americans are much concerned with methods of determining the requirements of nursing establishments, and some very interesting work is being undertaken by way of operational research at Johns Hopkins Hospital under the direction of Dr. Charles Flagle, a doctor of engineering at the university. Hospital administrators, conscious of rising hospital costs, are increasingly interested in determining the number of nurses that must be employed. This is a problem which affects us in England also.

Nurse-training is undertaken by university schools (15%), hospital schools of nursing and junior colleges—the latter corresponding to technical schools in England. In some hospitals there is a clear division between the nursing service under the director of nursing and nurse-training, over which the director of nurse education presides. In others the matron or director of nursing has the responsibility for both sides, discharged through assistant directors. As already mentioned, catering is not the responsibility of the nursing staff in American hospitals, nor is housekeeping, the department which is responsible for cleaning everywhere.

American nurses have a 40-hour week, and tend to work a three-shift system. The shortage of professional nurses has resulted in the recruitment of practical nurses and nursing aides. Practical nurses have a training period of from 12 to 15 months' duration and carry a State recognition (a licensed practical nurse is roughly the equivalent of the State-enrolled assistant nurse in this country). The training of the nursing aide (equivalent to our nursing auxiliary) varies from one to six months.

Nearly all American ward units have two-way loud-speaker systems which enable the patient to speak to the nursing station, in which there is a ward clerk if not a nurse. The ward clerk relieves the pressure on nursing personnel, and has been introduced generally in the United States. She deals with telephone inquiries, writes out requisitions of all kinds, enters up charts, and undertakes a large number of non-nursing duties. Patients appear to be well satisfied with the two-way loud-speaker system, though nurses with whom it was discussed did not regard it as a substitute for visiting the patient.

Payment for Medical Care

The Americans pay for their medical care mainly by voluntary health insurance, and 75% of the insurable population have some protection in this way. Even people so insured have, however, far less than complete protection against medical costs, and a recent study (Health Information Foundation, vol. VI, No. 6) suggests that most prevalent forms of health insurance cover only about one-third of the total costs of illness and health care to insured families. Nevertheless, health insurance, as underwritten by Blue Cross (doctors' fees), Blue Shield (hospital costs), and more recently commercial insurance companies, has increased enormously over the past few years. Indeed, health insurance forms a "fringe benefit" in many contracts between workers and employers. Increasingly the big unions enter into group arrangements with insurance companies to cover their members. Employee groups form the backbone of growth of insurance. In the mining and manufacturing industries 90% of workers and their dependants are covered by voluntary health insurance. Other industries vary from 33% in agriculture to 75% in transport and public utilities. In West Virginia the mineworkers have gone further and built 10 new hospitals in this rugged country. They are staffed by whole-time specialists and administered from Washington.

Commercial insurance appears to be gaining at the expense of the older non-profit forms of insurance and offers special contracts to low-risk populations. This may result, of course, in contracts being more difficult to make for high-risk groups of the population, such as old people. This is the one group needing adequate coverage, with their reduced incomes and high utilization rates for medical and hospital care; and voluntary health insurance of the population aged 65 and over has increased from 26% in 1952 to 39% in 1959. A recent survey conducted by the University of Chicago into voluntary health insurance among the aged showed that two-thirds of those aged 65 and over wished for an insurance which would cover all medical expenses, and half favoured Government insurance that would pay doctors' and hospital bills.

An interesting study sponsored by the Health Information is that of the Windsor (Ontario) Medical Services Plan. This contract covers all medical and surgical services, *x*-ray and special services, fees of consultants, services of anaesthetists and assistants at operations, preventive medical examinations and refractions, confinements, including antenatal and post-natal care, and consultations in the "office," home, or hospital. Tuberculosis, mental illness, drug addiction, and acute venereal disease are excluded and there is a waiting period before treatment of various conditions can begin. The Windsor plan is something which does not exist in quite this form in the United States. There is ample evidence that the American public is interested in having voluntary health insurance to cover a broader range of medical expenses than that designed to cover hospital expenses and doctors' fees for care in hospital.

Many sizable medical expenses occur outside hospital, and it is estimated that 20% of the total medical costs relate to care provided by doctors in the home and consulting-room.

In maternity care the trend is very much towards hospitalization. In 1935 63% of all babies were born outside hospitals. By 1956 95% of all babies were delivered in hospital and 97% of all registered births were attended by physicians, with an average of nine consultations for antenatal care. The duration of stay in hospital is between four and five days, the higher income groups staying longer. The average cost of physicians' service, hospital care, drugs, etc., in maternity hospitals was 75 guineas.

The cost of treatment in hospitals of all kinds is high, going up to $50 (about £18) a day, without doctors' fees or many of the extras like operating-room charges or costs of radiological or pathological investigations. The average duration of stay in hospital is short, and it is by this means in part that the hospital beds available have been able to cope with the tremendous demand for hospitalization which has occurred over the past 20 years.

General Practice

One of the most interesting features of American medicine is the tendency to group practice. The groups include general practitioners and specialists working often in centralized clinics indistinguishable from the health centres which were conceived under the National Health Service Act but which have never come into being. Some of these groups, like the Hospital Insurance Plan of New York, are prepayment schemes, the practitioners being wholly or partly in the plan. The premises of H.I.P. are modern and efficient, and provide complete investigatory and treatment facilities for out-patients. Most of the doctors in the partnerships hold hospital appointments and arrange in-patient treatment, for which separate payments are made. The quality of care under H.I.P. appeared to be high and hospitalization rates relatively low. Every attempt is made to avoid home calls and bring patients to the office or clinic. It is conceivable that the difficulty of parking cars—a national problem—may be in part responsible for this. In San Francisco, the Permanente plan "health visitors" on the hospital staff pay home visits first and the hospital doctor goes to the home only on the request of the health visitor.

The number of doctors as revealed by a study made in 1955 was such that a family doctor sees about 26 patients a day, most of them in his office: 17% of all doctors see more than 40 patients a day and 36% see more than 30. The average family doctor puts in about six hours a day on office calls and about an additional two hours a day on house calls. It appears that when allowance is made for hospital visits the estimated median working week comes to roughly 60 hours.

Two interesting experiments in the United States are the Montefiore Medical Group and the group practice at the Rip Van Winkle Clinic. The former is based on the Montefiore Hospital, New York, which was originally a hospital for chronic sick. It provides a comprehensive medical-care system based on the hospital. The practitioners are in fact specialist-trained in internal medicine and they are responsible for patients in the home, in the office, and in the hospital. Each full-time practitioner has between 1,200 and 1,500 patients over the age of 9 years. Children under 9 are looked after by paediatricians, and the maximum allocated to a paediatrician is 800. The family physician in the medical group practices only "adult medicine" and does not undertake paediatrics, minor surgery, obstetrics, orthopaedics, dermatology, or ophthalmology. For each of these an appropriate consultant is available. Another interesting feature of this medical group, which is financed by the Hospital Insurance Plan of New York, is the association as a team of a doctor, a social worker, and a public-health nurse. The team is supported by two groups of consultants—on the one hand the surgeons, obstetricians, ophthalmologists, and so on, who are part of the Montefiore Medical Group; and on the other hand a psychiatrist, a psychologist, a health educator, and a social scientist.

The Rip Van Winkle Clinic, in Columbia County, is a remarkably interesting experiment for providing diagnostic and treatment services in a relatively poor rural community. The staff of the clinic is made up of 17 specialists who are paid, on a salaried basis, from a pool created from fees charged on a fee-for-service basis. It should perhaps be mentioned that patients are increasingly coming in to the Rip Van Winkle scheme on a prepayment insurance plan, though this currently represents a very small percentage of the practice income. The group have a number of clinics scattered throughout the county, with one centrally, equipped adequately for physical diagnosis, *x*-ray and laboratory examination, physiotherapy, and dentistry.

The Rip Van Winkle Clinic has opened a cancer-detection centre which offers a complete examination for "the forgotten man in medicine, the so-called symptom-free adult." "This examination consists of the following procedures: complete history and physical examination; laboratory study (blood count, sedimentation rate, blood serologic test, urinalysis, and examination of stool for blood, ova, and parasites); *x*-ray films of chest abdomen and gall-bladder, gastro-intestinal series, and barium enema; oral examination by a dentist, including full-mouth and *x*-ray films; electrocardiogram, proctoscopy, Papanicolaou smear of cervix; laryngoscopy (indirect); visual examination with Orthorater; Cornell psychologic screening; and a conference with a psychiatrist (optional)."

The clinic also provides a mental health service with a staff of a psychiatrist, child psychiatrist, clinical psychologist, and psychiatric social worker, in an attempt to give comprehensive medical care.

General practitioners in the United States are said to be more specialized than in this country, but a random sample covering the whole of the States in 1956 showed that 73% of physicians interviewed declared that theirs was a general practice. It is true, nevertheless, that less than half the profession classified itself as practitioners without certification or special interest in a specialty.

One of the criticisms I heard most frequently was that we had divorced general practitioners from hospitals. This is true only in part, but it does mean that surgery in Great Britain, taken by and large, is no longer undertaken by general practitioners.

Medical Research

One of the most impressive things in the United States is the amount of money devoted to medical research. In 1957 this was in the order of $330,000,000, of which the Federal Government provided $186,000,000, involving the employment of about 20,000 professional research workers. There are indications that this sum will rise to $1,000,000,000 by 1970. Of this amount it is expected that the Federal Government will provide half and private philanthropy, industry, and endowments the remainder. These are, of course, astronomical figures compared with those for this country.

A most interesting place to visit is the National Institutes of Health in Washington. These are, in effect, seven hospitals within one curtilage. The institutes are devoted to the study of heart disease, metabolic disorders, cancer, mental health, neurological diseases, allergy and infectious diseases, and dental research. The 500 beds are served by a thousand laboratory rooms, and admission to hospital is secured only by patients suffering from the clinical conditions which the various institutes want to study. There is no charge for treatment, which must be very costly.

The budget of the National Institutes of Health for the year 1958 was $211,000,000. Of this amount, $147,000,000 was for extramural programmes, including research grants, training grants and fellowships, and grants to States for disease control and field investigations.

Visit to Puerto Rico

My trip ended with a visit to Puerto Rico. The population of this island, with a birth rate of 32 per thousand, increased by 18% between 1940 and 1950 and is now 2 million. Puerto Rico is rapidly becoming industrialized, and step by step with this development is endeavouring to regionalize its health and welfare agencies. The needs of the island have been surveyed and hospital and other medical facilities have been planned on a regional basis. There will be a teaching hospital in San Juan, with which will be closely associated a mental hospital and a hospital for chronic sick. The main specialist services will be located at San Juan in what will be known as the Medical Centre. Numbers of smaller health centres will provide limited

hospital care, public health and welfare services. These smaller health centres will send their major surgery, difficult midwifery cases, and patients requiring special diagnostic or treatment services to the district hospital. The district hospitals will have recourse to the Medical Centre teaching unit as needs be.

This is a fascinating experiment which could lead to a comprehensive system of medical care. There is great enthusiasm, but many have difficulties to be overcome, one of the chief of which is the provision of the necessary medical and ancillary personnel. Nevertheless, the start has been made, and here curative and preventive medicine, public health, and social services are being co-ordinated into a single system. This experiment, associated as it is with the American continent, where organized medicine is still an anathema, will be closely followed by all those interested in co-ordinated comprehensive medical care.

I am indebted to many doctors and administrators who gave me freely of their time, but particularly to Dr. Osler Petersen, then of the Rockefeller Foundation, for his wise guidance.

MEDICAL BIRTHDAY HONOURS

The names of the following members of the medical profession were included in a Birthday Honours List published in *Supplements* to the *London Gazette* on June 11.

K.C.M.G.

ALEXANDER MONTGOMERY WILSON RAE, C.M.G., M.D. Medical Adviser to the Secretary of State for the Colonies.

K.B.E. (*Military Division*)

CAMPION AUBREY RUMBALL, C.B.E., F.R.C.P., L.D.S., D.T.M.&H., D.P.M. Air Vice-Marshal, R.A.F. Honorary Physician to the Queen.

D.B.E. (*Civil Division*)

Lady MARY RANKEN HERRING, M.B., B.S. For social welfare services, especially in connexion with nursing organizations, in the State of Victoria, Australia.

Knighthood

ROBERT STEVENSON AITKEN, M.D., D.Phil., LL.D., F.R.C.P., F.R.C.P.Ed., F.R.A.C.P. Vice-Chancellor, University of Birmingham.

WALTER ERIC CHIESMAN, C.B., M.D., F.R.C.P. Medical Adviser, H.M. Treasury.

JOHN SAMUEL RICHARDSON, M.V.O., M.D., F.R.C.P. Physician, St. Thomas's Hospital.

GEORGE DOUGLAS ROBB, C.M.G., M.D., Ch.M., F.R.C.S., F.R.A.C.S. Consulting Surgeon, Green Lane Hospital, Auckland, New Zealand. Member, New Zealand Medical Council and New Zealand Medical Research Council. Nominated President-elect of the British Medical Association for the year 1961–2.

BENJAMIN WILLIAM RYCROFT, O.B.E., M.D., F.R.C.S., D.O.M.S. Oculist to H.R.H. the Princess Royal. Consulting Ophthalmic Surgeon to Corneo-plastic Unit, Queen Victoria Hospital, East Grinstead; the Plastic Unit of the Kent County Ophthalmic and Aural Hospital; and the Sussex Eye Hospital.

C.B. (*Military Division*)

GILBERT THOMAS LANCELOT ARCHER, M.B., B.Ch., F.R.C.P.I. Major-General, late R.A.M.C. Honorary Surgeon to the Queen.

WILLIAM DILLON HUGHES, C.B.E., M.D., F.R.C.P.I., D.T.M.&H. Major-General, late R.A.M.C. Honorary Physician to the Queen.

WILLIAM ROBERT SILVESTER PANCKRIDGE, M.R.C.S., L.R.C.P. Surgeon Vice-Admiral. Honorary Physician to the Queen.

DERMOT FRANCIS WALSH, O.B.E., M.B., B.Ch., F.R.C.S.Ed. Surgeon Rear-Admiral. Honorary Surgeon to the Queen.

C.B.E. (*Military Division*)

LESLIE REGINALD HEBER KEATINGE, O.B.E., M.B., B.Ch. Brigadier, late R.A.M.C.

GERARD WARD MCALEER, M.B., B.Ch., D.T.M.&H. Air Commodore, R.A.F. Honorary Physician to the Queen.

JOHN GEORGE GLYN WHITE, O.B.E., E.D., M.B., B.S. Colonel, Royal Australian Army Medical Corps.

C.B.E. (*Civil Division*)

DAVID BROWN, M.B., Ch.B. For political and public services in Bootle.

LAWRENCE JOHN CLAPHAM, M.D., D.P.H., D.T.M.&H. Director of Medical Services, North Borneo.

JAMES GRAHAM, M.B., Ch.B. Senior Administrative Medical Officer, North-East Metropolitan Regional Hospital Board.

IAN DINGWALL GRANT, M.D. Lately President, College of General Practitioners. Vice-President, British Medical Association.

LUDWIG GUTTMANN, O.B.E., M.D., F.R.C.P. Director, National Spinal Injuries Centre, Stoke Mandeville Hospital, Aylesbury.

HENRY MCLORINAN, M.B., B.S., F.R.A.C.P., of Fairfield, Victoria, Australia. In recognition of his work in the field of preventive medicine.

MARTIN AMSLER RUSHTON, M.D., F.D.S.R.C.S., F.D.S. R.C.S.Ed. Professor of Dental Medicine in the University of London.

M.V.O. (*Fourth Class*)

HERBERT BRIAN KELLY, M.D., M.R.C.P. Wing Commander, R.A.F.

O.B.E. (*Military Division*)

CLIFFORD VIVIAN HARRIES, M.R.C.S., L.R.C.P., L.D.S., D.P.H., D.I.H. Surgeon Commander, R.N.

ROBERT ADAMS MCKEOWN, M.B., B.Ch. Surgeon Commander, R.N.R.

JOHN ERSKINE MALCOLM, M.B., Ch.B., F.R.C.S. Wing Commander, R.A.F.

O.B.E. (*Civil Division*)

JOHN ADAM, M.B., Ch.B. Regional Medical Officer, Ministry of Health.

WLADISLAW DERING, M.D. Senior Medical Officer (Surgical), Somaliland Protectorate.

JOHN DIXON, L.R.C.P.&S.Ed., L.R.F.P.S.Glasg. Chairman, St. Albans Medical Board.

HUGH RICHARD JARVIS DONALD, B.M., B.Ch., M.R.C.P. Physician, Christchurch Public Hospital, New Zealand.

CYRIL FORTUNE, M.D., F.R.A.C.P. For services to the Blood Transfusion Service in the State of Western Australia.

GEOFFREY DESMOND GORDON, M.R.C.S., L.R.C.P., D.T.M.&H., D.O.M.S. Senior Medical Officer, Ministry of Pensions and National Insurance.

ROBERT FRITZ HERRIES HINRICHSEN, M.D., F.R.C.S., F.R.C.S.Ed. Medical Director, Strangers' Hospital, Rio de Janeiro, Brazil.

LEONARD CATESBY HUGGINS, M.B., Ch.B. Medical Officer and Bacteriologist (Senior Surgeon), Bahamas.

TREVOR CLAUDE JAMES, M.B., B.S. Commissioner of the St. John Ambulance Brigade in the State of Tasmania.

WINIFRED BARBARA MEREDITH, M.B., B.S. Director of Maternal, Infant and Pre-school Welfare, Department of Health, State of Victoria, Australia.

THOMAS MCCOWAT MONTFORD, M.B., Ch.B. Chairman, Leicestershire and Rutland Executive Council, National Health Service.

MILES PARKES, M.B., Ch.B. Vice-Chairman, Cheshire Executive Council, National Health Service.

CHARLES EMANUEL WILLIAMS, M.D., F.R.A.C.S. A medical practitioner of Mackay, State of Queensland, Australia.

M.B.E. (*Military Division*)

DONALD CAMPBELL MCNUTT, M.B., Ch.B. Surgeon Lieutenant-Commander, R.N.

M.B.E. (*Civil Division*)

LEONARD EDWARD ARNOLD, Pathologist, Police Department, Jamaica.

HECTOR MACKAY CALDER, D.S.O., M.C., M.D. Lately Member, Glasgow National Service Medical Board.

WALTER WATSON FEATHER, M.B., Ch.M. Medical Superintendent, Roma Hospitals Board, State of Queensland, Australia.

THOMAS DUNCAN GOULD, L.R.C.P.&S.Ed., L.R.F.P.S.Glasg., L.D.S. British subject resident in Belgium.

MARY RAE KEYMER, M.B., Ch.B. British subject resident in the Sudan.

MURIEL MILLICENT MANLEY, M.B., B.S. For public services in Jamaica.

EDWARD HAMMOND WILLIAMS, M.B., B.S. For public services in Uganda.

SIR WILLIAM COATES, 100

Sir William Coates, who qualified in 1881 and joined the British Medical Association in the following year, celebrated his 100th birthday on June 14. We are happy to offer him our congratulations and those of all his fellow members of the B.M.A. His record of service to the volunteer movement of the Army is second to none in the medical profession. In Manchester, where he lives and where he practised until a few years ago, he has always been regarded as an outstanding personality, and that is something to be proud of in a city so brimming with talent.

A native of Worksop, William Coates qualified from the London Hospital, and after holding resident posts there he settled in Manchester in 1884. Joining the Volunteer Rifle Corps as a surgeon, he later became adjutant of the Manchester Company of the Volunteer Medical Staff Corps, the first non-Regular medical unit outside London. In 1909, under Lord Haldane's scheme for the reorganization of the Army, he formed Field Ambulance No. 18 of the R.A.M.C., attached to the 6th Division of the Regular Army, becoming its chief administrative officer and its honorary colonel in 1914. During the first world war William Coates served as A.D.M.S. in Western Command. After the war he again gave an exemplary lead in the organization of measures to safeguard the welfare of those whose wounds had caused total disablement. He was also an energetic and influential supporter of the V.A.D. movement, being chairman of the East Lancashire Joint Committee of the Order of St. John and of the British Red Cross Society.

Sir William Coates was appointed C.B.E. in 1920 and knighted in 1930. Twelve years before this he was appointed a Commander of the Bath (Military Division), having already in 1908 been appointed to the Civil Division of the Order. In 1930 also he became a deputy lieutenant for the County Palatine of Lancaster.

Honour also came to him from his own profession, for after serving as secretary of the Manchester Medical Society he was elected its president in 1909. His presidential address on "The Duty of the Medical Profession in the Prevention of National Deterioration" was published in this journal, as were other papers he wrote on specifically clinical subjects. Much of the success of the Annual Meeting of the B.M.A. in Manchester in 1902 was due to his work as local general secretary. His membership of the B.M.A. for 78 years is thought to constitute a record, and he is the oldest Fellow of the Royal College of Surgeons, to which he was elected in 1930.

Sir William has lived in the same house at Moss Side for 69 years. Unhappily he has lost his sight, but that does not prevent him from taking a keen interest in national and local affairs, particularly in the R.A.M.C. and the Territorial Army. Doctors will wish to salute a colleague who has for so long given such distinguished service to his country and to his profession.

To-day's Drugs

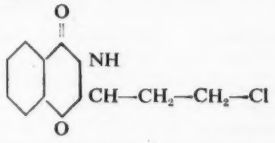
With the help of expert contributors we publish below notes on a selection of drugs in common use.

Chlorthenoxazin

"Valtorin" (Pfizer).

Valtorin tablets contain 200 mg. phenacetin and 250 mg. chlorthenoxazin.

Chemistry.—Chlorthenoxazin is 2-(β-chlorethyl 1)-2,3-dihydro-4-oxo-(benzo-1-3 oxazin), and has the following structural formula:



Pharmacology.—Phenacetin is a familiar member of the antipyretic analgesic group of drugs, and has been in clinical use since 1887. The other ingredient is chlorthenoxazin, which is now introduced. This is also an antipyretic analgesic of a type similar to aspirin and phenacetin. The duration of action of chlorthenoxazin is 50% longer than that of aspirin.

Therapy.—In man chlorthenoxazin has been found to have about the same analgesic effect as paracetamol, and valtorin—i.e., phenacetin plus chlorthenoxazin—about the same effect as compound codeine tablets.[1] The dose of valtorin is two tablets three times a day, and it may be possible to reduce the dose after three or four days owing to some cumulation. Valtorin is supplied as tablets which dissolve pleasantly in the mouth, so that there is no need to seek water to drink with them—a slight, but to some people definite, advantage. It would seem that valtorin is worth trying for patients who either are not helped by the usual mild analgesics or who develop gastro-intestinal side-effects with them.

Toxicity. — Phenacetin may cause haemolysis and methaemoglobinaemia, but this is unlikely to occur if the above dosage is not exceeded. Chlorthenoxazin has not, up to the present, been found to cause any serious toxic effects. Transient nausea may occur.

When new analgesics which do not cause occult bleeding from the alimentary tract are introduced, it is commonly suggested that they should be used routinely instead of aspirin, for aspirin has been reported to cause the appearance of occult blood in the faeces of some patients, the proportion varying considerably in different series of patients. Such claims must be measured against the long history of aspirin, which, in view of the immense amounts taken, seems to be an unusually safe drug.

N.H.S. Basic Price.—100 tabs., 16s. 8d.

REFERENCE

1 Wilson, D., Kendall, P. H., and Pawsey, P. M., *Brit. med. J.*, 1960, 1, 36.

Training Made Easier deals with the two basic questions facing anyone concerned with training manual operatives: "What do trainees have to learn?", "How can they be helped to learn?" In doing so, it shows how the results of four recent studies can help industry to find the answers. It emphasizes the need for careful planning before setting up systematic training, for which the essentials are: Observe how the experienced operator does the job and analyse in detail the mental and physical components of his performance. Fit the training method to the job. Get expert advice. (*Training Made Easier*, published for the Department of Scientific and Industrial Research by H.M.S.O., price 2s., by post 2s. 2d.)

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Approved Names

SIR,—We are urged at our medical schools and by the authorities to prescribe drugs by officially approved names rather than trade names. In your issue for June 4 (p. 1731) is a list of 20 new "approved names," and 17 trade names are mentioned in the list. I have done a little research on these with the following results:

Approved Names	*Syllables*	*Letters*
Minimum	4	11
Average	4.95	13.15
Trade Names		
Average	2.28	7.35
Maximum	4*	9

*Only 1 trade name out of 17 had more than three syllables.

The approved names are about twice as long as the trade names, and, I should say, without exception the trade names are easier to write, to say, and to remember. This is a serious consideration for prescribers, nurses, and others. Who is going to prescribe thioproparazine methanesulphonate (or even thioproperazin. methanesulphonat.) if "majeptil" is available? I suggest that, if a little thought is used, no single drug need have more than three syllables in its name (say 8 letters). These long names are mostly a vain attempt to suggest chemical structure, which should be abandoned when it cannot be done briefly. The saving in ink, time, money, and confusion would be enormous.—I am, etc.,

Uxbridge. R. B. O. RICHARDS.

Vacuum Extractor in Obstetrics

SIR,—I have read with great interest the article by Mr. J. A. Chalmers and Dr. R. J. Fothergill (June 4, p. 1684) on the use of the vacuum extractor or "ventouse" in obstetrics. Under the direction of Professor Ian Donald at the Glasgow Royal Maternity Hospital, Rottenrow, the vacuum extractor has been used in 19 cases during the last year. The instrument used was Malmström's and the technique was as described by him.

Pudendal block anaesthesia was used in 15 cases, local infiltration of the perineum in 1, and general anaesthesia in 3. In 7 cases the instrument was applied before and in 12 cases after full dilatation of the cervix. The indications for the use of the instrument were: foetal distress in the first stage, 2; foetal distress in the second stage, 2; prolonged hypotonic first stage, 5; delay in the second stage, 9; and compound presentation (hand and head), 1. In only 10 cases was it possible to complete delivery with the extractor; in 8 delivery was completed with forceps and in one by caesarean section.

It was clear from the outset that the vacuum extractor offered a means of hastening the end of the normal first stage and could be used instead of low forceps in the second stage. However, as nearly all low-forceps and mid-forceps deliveries in this unit had been performed under local anaesthesia for some years past, it was felt that an alternative to low-forceps delivery was not a particularly long-felt need and that it would be more interesting to explore the possibilities of the instrument in more difficult cases. Cases of dystocia due to mechanical difficulties abound in the Royal Maternity Hospital, for most of the hospital's normal cases are filtered off to an annexe of 75 beds. Cephalo-pelvic disproportion is still common in Glasgow. Mr. Chalmers and Dr. Fothergill quote cephalo-pelvic disproportion as a contraindication to the use of *la ventouse* and state that forceps delivery was required in their series when more than a minor degree of disproportion was present.

The reason for the large failure-rate in our small series is that the vacuum extractor was not sufficiently powerful to effect delivery in these cases. We have shown experimentally in the freshly stillborn foetus that the maximum force which can be exerted by the vacuum extractor is in the region of 21 lb. (9.6 kg.); when a greater force is used the cup will pull off. Yet there are many occasions when delivery requires a greater force than 21 lb. and no injury to mother or child results; these are the real cases of second stage delay due to mechanical factors, and it is our experience that they are much more common in practice here than is generally imagined. It is extremely difficult to forecast, in such cases, how much force will be required; in cases where there is reasonable doubt of the outcome, "trial of forceps" is employed, but "trial of vacuum extraction" would seem to have little place, for a patient in whom the extractor fails may be easily delivered by the forceps.

One of the most interesting features of the instrument is that it can be applied before full dilatation of the cervix, and perhaps its greatest use will be as an alternative to caesarean section or forceps in cases where the need for delivery becomes urgent late in the first stage. Yet it would be unfortunate if the instrument were to lead to a revival of the old desire for vaginal delivery at all costs; for example, one cannot help feeling that Case 87 of Mr. Chalmers and Dr. Fothergill, where delivery was completed by incision of the cervix and ventouse extraction, might have been just as safely delivered by caesarean section.

Our preliminary experience with the vacuum extractor has suggested to us that it is a suitable alternative to low-forceps but by no means an alternative to mid-forceps delivery. It has also several other interesting possibilities still to be explored. We think that it is still too early to make *Toujours la ventouse* our slogan. Rapid, easy deliveries seem not to traumatize the child, but prolonged traction may result in abrasion of the scalp (the complication on whose account Antoine abandoned weight traction with the instrument in Vienna), which is not a trivial matter in these days of neonatal infections with organisms resistant to antibiotics.

We look forward to further experience with *la ventouse*, which should be welcomed, like all mechanical aids to delivery, but with suitable caution.—I am, etc.,

Glasgow. JAMES WILLOCKS.

Premedication

SIR,—I should like to comment on Professor W. W. Mushin's advice regarding premedication for operative obstetric procedures (May 21, p. 1558). I am unwilling to support his remarks about the place of the phenothiazine derivatives. These drugs he has included with the opiates and barbiturates in the statement, "All the drugs already described cross the placenta rapidly, and within minutes circulate in the foetal blood in the same concentration as in the mother's. The baby at the time of birth will therefore be nearly as sedated as the mother at that moment."

As far as chlorpromazine is concerned, the obstetric objection to the drug lies in the hypotension which it is capable of producing, together with the facts that

the degree of maternal sedation is unpredictable and that the duration of labour may be increased. On the other hand, promethazine is a useful member of the obstetric anaesthetist's formulary, particularly in allaying the anxiety of mothers awaiting elective procedures, such as caesarean section. I have found that promethazine 50 mg. given by intramuscular injection one and a half hours pre-operatively provides adequate maternal sedation without affecting the foetus.

Adelman *et al.*[1] made attempts to measure the concentrations of promethazine in maternal and foetal-cord blood samples and found that, in spite of maternal venous-blood levels of 200 μg./100 ml., none was detectable in cord blood. Behn *et al.*[2] have, however, demonstrated the presence of phenothiazine derivatives in the urine of newborn infants by employing photometric and paper chromatographic techniques. The amounts of these drugs which passed from mother to baby varied from 0.5% to 1% of the dose given to the mother. The findings of Carroll and Moir[3] support my own clinical impressions that there are few contraindications to the use of promethazine, that it enters the placental circulation in insignificant amounts, and that it has no adverse effect on the foetus.—I am, etc.,

T. W. BAILLIE.

The Glasgow Royal Maternity and Women's Hospital, Glasgow, C.4.

REFERENCES

1 Adelman, M. H., Fisch, H., Jacobson, E., and Katz, J., *Anesthesiology*, 1958, **19**, 93.
2 Behn, W., Frahm, M., and Fretwurst, E., *Int. Abstr. biol. Sci.*, 1957, **5**, 343.
3 Carroll, J. J., and Moir, R. S., *J. Amer. med. Ass.*, 1958, **168**, 2218.

Vomiting after Nitrous Oxide

SIR,—The very interesting statistical study by Dr. R. I. Bodman and his colleagues of vomiting by out-patients after nitrous-oxide anaesthesia (April 30, p. 1327) is, to my mind, marred by a serious omission. The authors did not study the most important variable at all—that is, the degree of hypoxia to which these patients may have been subjected.

Standard British texts on anaesthesia (e.g., *General Anaesthesia*, edited by Frankis T. Evans and Cecil Gray, 1959, Butterworth, London) still recommend induction with 100% nitrous oxide. For example, the textbook cited above, on page 12 of Volume 2, after noting that nitrous oxide alone is given at first, to clear nitrogen and oxygen from the lungs, states that, "As soon as automatic breathing is established, oxygen is added, at first in small quantity. The mistake most often made by the novice is to give too much oxygen at the beginning of anaesthesia. . . ." Techniques in which less than 20% by volume of oxygen is administered to the patient can only lead to acute anoxia. Anoxia is one of the most potent causes of nausea and vomiting, as the early workers in the field of "mountain sickness" were able to demonstrate in the last century.

Dr. Bodman and his colleagues do not give any description of the methods by which anaesthesia was induced and maintained in their patients, and one can only infer that they followed standard British teaching. The fact that the incidence of vomiting increased in a linear fashion in relation to duration of anaesthesia seems to support this suspicion. As the presence of hypoxia is a factor almost always directly controllable by the anaesthetist, it seems a pity that this parameter could not also have been either controlled or recorded. —I am, etc.,

C. S. JONES.

Department of Anaesthesia, University of Capetown, South Africa.

Treatment of Hydrocephalus

SIR,—Referring to your annotation on the Spitz–Holter valve in hydrocephalus (May 7, p. 1419), we question that an entirely fair picture of the problem involved is given and consider that some of the conclusions you have drawn from K. M. Laurence's[1] excellent article on the natural history of hydrocephalus are misleading. In this article 182 untreated cases of hydrocephalus collected in the pre-Spitz–Holter-valve era were followed up and it was found that 81 (44.5%) were alive and had undergone spontaneous arrest, but that only 33 (18.1% of 182) had a normal I.Q. (greater than 85); 89 (48.8% of 182) were dead.

Any worthwhile operation for hydrocephalus should therefore achieve: (1) arrest in more than 44.5% of the cases; (2) more than 18.1% of the operated children should have normal intelligence; and (3) the operative mortality should be less than 48.8%. To date, more than 5,000 Spitz–Holtzer valves have been inserted[2] and various surgeons[3–6] reporting large series of cases operated upon have shown arrest of the condition in at least 80%. These results are similar to those obtained in our small series of 80 cases operated upon by the Spitz method during the last 2½ years—our mortality rate is approximately 10%.

We must also consider another important factor: nearly all children with progressive hydrocephalus in this region now undergo operation within the first few months of life and the size of their heads never approaches the proportions often seen in children with natural arrest of the condition. While it is clear from Laurence's work that intelligence bears little relationship to the thickness of the cortex, there is no doubt that spasticity resulting from damage to the pyramidal tracts is often found in advanced cases. Early insertion of the Spitz–Holter valve will therefore not only save many lives but will also ensure that the survivors are not handicapped by spasticity and the weight of an enormous head. We have seen no deterioration of intelligence following operation, and, although it is too early to make a definite statement, we are of the opinion that the percentage of operated children with normal intelligence will be very much greater than the 18.1% which one can expect in untreated cases.

The most important fact that emerges from Laurence's work is the finding that spontaneous arrest occurs in most cases within the first three years of the disease. Any operation which tides the patient over this critical period might therefore reasonably be expected to produce lasting relief.—We are, etc.,

P. P. RICKHAM.
J. R. ROBERTS.

Liverpool.

REFERENCES

1 Laurence, K. M., *Lancet*, 1958, **2**, 1152.
2 Holter, J. Personal communication.
3 Spitz, E. B., *Pediat. Clin. N. Amer.*, 1959, **6**, 1215.
4 Carrington, K. W., *J. Mich. med. Soc.*, 1959, **58**, 373.
5 MacNab, G. H., in an address given to the Society of Britain Neurological Surgeons, December, 1958.
6 Sayers, M. P. Communication circulated by the Holter Company.

Mental Health Tribunals

SIR,—In 1957 a girl and in 1958 a young man, having escaped from mental institutions, appeared before the then Lord Chief Justice of England and appealed to him for their freedom. This he granted them, but not before he had made some scathing comments about the system which allowed such persons to be unjustifiably incarcerated. It so happens that I have come to know well two men who have been held in mental institutions for ten and seventeen years respectively. Both have now regained their freedom by means of our courts of justice.

Before the passing of the Education Act of 1944 it was sometimes the custom of certain councils which had no facilities for the education of "educationally difficult children" to send them, for convenience sake, to institutions for the mentally defective. It would seem that with the passing of years it was sometimes forgotten that these children had never been certified but were treated as if they had. This is what happened to the first of my two cases. The second was committed by a juvenile court to an institution for mental defectives without his appearing before the court in question. In my many talks with these two men I have not been able to detect any signs of mental deficiency, rather would I have thought that they were superior to their companions in intelligence and knowledge of current affairs. They would appear to lack, and who could wonder after such an upbringing, a proper sense of responsibility and of altruism.

It was first the intention of the Minister to include general practitioners amongst the medical members of the Mental Health Tribunals which are about to be formed, but, I understand, he has now changed his mind and only psychiatrists are to be included, so that if in our mental institutions there are any more unfortunates, such as the above-mentioned four, who have not as yet been able to obtain their freedom, they will still from the medical aspect have to remain at the mercy of their gaolers, the psychiatrists. Specialism is not always the optimum.—I am, etc.,

Topsham, near Exeter. F. E. GRAHAM-BONNALIE.

Thioridazine

SIR,—I note that thioridazine ("melleril") is now available in this country. Certain claims regarding the relative absence of side-effects and toxicity of this phenothiazine derivative cannot in my own experience be substantiated.

A pilot study was made on six male schizophrenics, aged 40–60 years, who had been in hospital for ten or more years and had no clinically relevant physical disorder. None had previously received any phenothiazine derivative; none had any history of hepatitis (either viral or allergic) and there there was no biochemical evidence of liver dysfunction; no hypersensitivity, idiosyncrasy, or drug eruptions had occurred with either barbiturates or succinylcholine. Thioridazine was administered in doses of 75 mg. *per diem* in divided doses, and routine haematological studies, urinalysis, and baseline recordings of the influence of posture on the blood pressure were carried out.

Ten days later, three cases had developed light sensitization and peri-orbital oedema, clinically indistinguishable from chlorpromazine photosensitization; four cases exhibited a pseudo-Parkinsonian tremor (drug-induced extrapyramidal syndrome); and all six showed a transient polymorphonuclear leucocytosis (12,000–15,000 per c.mm.) between the fifth and tenth days of therapy.

While substitution in the 2-position of the tricyclic phenothiazine nucleus is academically justifiable and commercially profitable, I think that previous experience with many other allegedly selective psycho-sedative analogues has ultimately led to the conclusion that they are equipotent and equitoxic when subsequently reviewed critically with chlorpromazine as the prototype molecule. Pharmacologically and therapeutically there is little to choose between these congeners except in price.—I am, etc.,

Middlewood Hospital, Sheffield, 6. DOUGLAS A. KENT.

Pituitary Irradiation

SIR,—I have read with great interest the various publications about surgical implantation of radioactive substances into the pituitary gland. I wonder, though, whether not too much trouble is taken in perfecting this relatively complicated and sometimes dangerous procedure: it is much easier to introduce a suitably filtered radium tube, which is fitted to the end of a probe, to the top of the pharynx. The mucous membrane of the nose is anaesthetized, the distance between nares and top of the pharynx measured with a graduated probe. Now the probe with the radium tube is inserted into the nose, and, when the back of the pharynx has been reached, the handle is lowered, which results in the lifting of the tube towards the top of the pharynx and within about 2 cm. from the pituitary gland. Any amount of gamma-radiation can be delivered in this way.

I have used this method, as described by my father in 1923, for some twenty years in cases of diabetes insipidus, acromegaly, pituitary tumours, and certain types of uterine bleeding. Though the mucous membrane receives a great amount of irradiation, no serious side-effects have been observed.—I am, etc.,

London, S.W.3. E. F. BLUMBERG.

Uterine Haemorrhage due to Abnormal Vessels

SIR,—The interesting paper by Dr. R. Salm and Mr. P. N. Simons (May 21, p. 1534) evokes memories of a patient who gave rise to not a little anxiety some years ago.

She was a primigravida, aged 33, who was admitted to hospital as an emergency some days past term because of poor progress in the first stage of labour. She eventually had a caesarean section on account of supervening foetal distress, a live child being delivered. At the operation, which proceeded quite normally, there were no untoward findings.

On the ninth day of the puerperium the patient had a sudden uterine haemorrhage. The uterus was explored without result under general anaesthesia, and the bleeding quickly subsided. Nineteen days after operation, however, a severe uterine haemorrhage occurred, and, though a blood-transfusion was commenced almost immediately, even bilateral drips going full out were proving inadequate in sustaining a reasonable blood-pressure. An emergency hysterectomy had to be undertaken; when the patient returned to the ward, 7 pints (4 litres) of blood had been administered within about 4 hours of the beginning of the haemorrhage. The excised uterus contained several small, softened, subserous fundal fibroids, which scarcely disrupted its outline. The pathologist found them to be a good deal more extensive, however, and reported that the endometrium overlying a submucous fibroid contained some large vascular channels. These were presumed to have been the source of the bleeding.

Many gynaecologists must have had dealings with dramatic cases of "dysfunctional" uterine haemorrhage, some of them quite likely after pregnancy, which in the

end made hysterectomy imperative. Our next-door neighbours, the urologists, carry out renal arteriography via the aorta with impunity. Why not, therefore, uterine arteriography? I believe Dr. Salm and Mr. Simons have made a valuable contribution in placing vascular anomalies of the uterus on the map. It would be a further and a thoroughly desirable step forward if the bleeding-points could be accurately located radiologically and dealt with locally, thus conserving reproductive function in these often quite young women.—I am, etc.,

Liverpool, 7. E. G. JONAS.

Is Trichomonal Infestation Venereal?

SIR,—Drs. R. D. Catterall and C. S. Nicol (April 16, p. 1177) and Dr. Nicol (May 28, p. 1654) and Dr. L. Watt and Professor H. C. McLaren (May 14, pp. 1502 and 1503) and Dr. Elisabeth Rees (May 28, p. 1655) all discuss the problem of whether and when patients with undiagnosed vaginal discharge should be referred to clinics for venereal disease, and they make specific reference to trichomonal infestation.

We believe that the question of terminology here is of the utmost importance. The venereal diseases were named in the Public Health (Venereal Disease) Regulations of 1916 as syphilis, soft sore, and gonorrhoea. There is no argument that infestation with *Trichomonas vaginalis* is acquired by sexual intercourse in most cases, and is in that sense venereal, but it is not "V.D." in the narrow sense of the term to which the public are accustomed. At the present time more than half of the patients attending clinics for venereal diseases are suffering from conditions distinct from the three named illnesses. These conditions include genital infection such as non-gonococcal urethritis, moniliasis, and trichomoniasis.

The simple case of discharge presenting at a gynaecological clinic may well be diagnosed and cured at a single attendance. On the other hand, detailed investigation, treatment, and follow-up may be required. The exclusion of gonorrhoea, so often a latent disease in women, may require repeated tests. The average gynaecological clinic is not equipped adequately, nor has its personnel sufficient time, to investigate thoroughly the marital partners or the contacts in a less permanent sexual union. It is natural for such cases to be referred to the department which primarily specializes in this field of work and is fully equipped to undertake it.

We feel that the term "Venereal Diseases," when obviously applied to centres which must deal with all the conditions transmitted by sexual intercourse, impedes the work that is done there. At this hospital, as at others, steps have been taken to widen the service provided by the Special Treatment Centre and to lessen any possible stigma attached to its patients. Clinics here are held in an annexe which is shared for occasional sessions by specialists in other fields. Patients referred to the venereologist are referred to him by his name at "The Annexe." A mid-day session is primarily reserved for the investigation of patients in whose cases problems seem likely to arise, and, with this management, social difficulties have been very few.

It seems to us to be important, especially in the investigation of trichomoniasis, that the sexual partners should be seen by the same doctor, and that he tells them that the condition is a simple "inflammation" that can be passed at intercourse. Since the venereologist treats so much more than syphilis, gonorrhoea, and chancroid, we wonder whether it is not perhaps time not only to change the name of the department in which he works but also the name of his specialty.—We are, etc.,

Oldchurch Hospital, Romford. ELLIOT E. PHILIPP. ERIC DUNLOP.

Delay in the Third Stage

SIR,—I would endorse the observations of Dr. P. M. Elwin (May 21, p. 1569) regarding the Brandt–Andrews technique of expressing the placenta, but in addition would suggest using oxytocin rather than ergometrine. Since observing the results using oxytocin in the third stage I have adopted this procedure routinely.

Oxytocin (10 i.u.) is given intramuscularly at the end of the second stage, the exact timing being unimportant. If the placenta has not separated within ten minutes the Brandt–Andrews manœuvre is used. If unsuccessful it is repeated in several minutes, and if this attempt fails the anaesthetist is sent for for a manual removal. Since, in a personal series of 266 consecutive deliveries to date, there have been three manual removals and five post-partum haemorrhages; one of each occurred in a patient who had a retained placenta succenturiata. In all the remainder the third stage was completed within twenty minutes, the great majority in less than twelve minutes. No disadvantages were noted from the use of oxytocin in this dosage; there were no complaints of excessive contractions, and the placentas retained were adherent but separable. Presumably, an unsuspected twin might be delivered more rapidly and with less risk of anoxia than might be the case with ergometrine, but of this we have yet no experience. As with ergometrine, it seems that the blood loss during the third stage, and perhaps also after, is reduced. A review of about 800 other cases here shows similar results—namely, a shortened third stage, no unnecessary anaesthetics, and no ill effects.—I am, etc.,

U.S. Army Hospital (Paris), Neuilly-sur-Seine, France. A. V. GRASSET.

SIR,—May I say how much I am in agreement with Dr. P. M. Elwin (May 21, p. 1569)? I have used the Brandt–Andrews technique in over 40 deliveries in the past eighteen months and found it most satisfactory. After giving intravenous ergometrine I take over the third stage as soon as the midwife has divided the cord. The third stage is completed in a few minutes with minimal blood loss.—I am, etc.,

Redhill. KEVIN KELLY.

Spiritual Healing in Hospitals

SIR,—Surely the question whether or not spiritual healers should be welcomed in hospitals depends upon their attitude to the treatment which hospitals are provided to give. It is said that Cromwell exhorted his soldiers to trust in the Lord and keep their powder dry. As far as I know the societies associated with the Churches' Council of Healing and a large proportion of medical practitioners adopt a similar attitude in their fight against disease. They believe that all must be done to make the patient's physical condition as good as possible by surgery and medical treatment (doctors' special job), but they also recognize the immense value

of the patient's morale, his confidence and will to survive, which Christians would attribute to a faith in a kind God.

There are scientific-minded doctors who place little or no value on faith or morale. They would merely advise "Keeping the powder dry." On the other hand there are spiritual healers who, like the Christian Scientists, think that all physical treatment is positively wicked, as showing lack of faith. Their advice would be to "Trust in the Lord and throw your powder away." At a public demonstration of spiritual healing a few years ago I heard a champion of the National Federation of Spiritual Healers thoroughly castigate a patient with an arthritic knee because he had previously had a cartilage excised. The healer told him that he could not expect any cure from the Almighty since he had shown such lack of faith in the past as to allow a surgeon to mutilate his joint. Such spiritual healers are perfectly entitled to their opinions, in defence of which some are willing to go to prison, and we may even admire them for this. It does, however, seem anomalous to let them perambulate in hospitals which are maintained by the taxpayer at great expense for the express purpose of excising cartilages and other more complicated treatments, all of which they condemn.—I am, etc.,

Norwich. B. E. JERWOOD.

SIR,—Dr. V. Cotton Cornwall, in his official capacity as president of the Regional Hospitals' Consultants and Specialists Association, has written to the medical press (May 28, p. 1652) criticizing the permissions granted to spiritual healers to attend the sick in hospitals (under special circumstances), and I therefore assume he has presented his strongest case against this new practice.

His first argument is that the Bishop of Lichfield said that the Churches' Council of Healing does not recognize the National Federation of Spiritual Healers. Does this comprise a valid objection? The Federation is undenominational, and its constitution prevents its affiliation with any other religious bodies. The gift of healing can never become the prerogative of any religion, and certainly not that of the Churches' Council of Healing. To suggest that healers should be debarred from helping the sick, because the Churches' Council does not recognize us, is surely the weakest of arguments.

The learned doctor next raises the point that the act of a doctor giving permission for a spiritual healer to attend his patients may lay him open to a charge of "covering." We have taken a Queen's counsel's advice on this matter, and it is his opinion that the granting of such permission does not violate the rule of "covering" or "association," neither does it imply acceptance by the doctor of the efficacy of spiritual healing.

Those are the only objections mentioned by Dr. Cotton Cornwall, but he adds that members of the National Federation "should not be given special privileges, nor granted consultations on treatment with medical staff." We are not asking for special privileges. Spiritual healing is part of our common religious belief. It is a divine act. Therefore the attendance of a spiritual healer upon a patient has the same significance as that enjoyed by ministers of religion, who visit the sick for the purpose of prayerful intercession and the laying-on of hands. That is all we wish to do. We are not asking for consultations with the doctors as a right or privilege. Surely there can be no harm in a doctor, if he wishes, to talk about a patient's condition with a healer, any more than when he discusses this with the patient's relatives or friends. It seems that some doctors are trying to create difficulties when there are none, and inventing suppositionary circumstances which may never arise.

The main objection seems to be that we healers shall be giving a spiritual healing "treatment." Of course we shall, but let us get this in its right perspective. We say that a divine power or healing force is transmitted to the patient through our gift of healing. There is abundant evidence to prove that this is so. Surely this is what the members of the Churches' Council of Healing seeks too. The difference is that the healer possesses the gift of healing, and unfortunately the average parsons do not. Why deny to those patients who desire to benefit in this way the help that we can give? Spiritual healing treatment is not in opposition to medical practice—on the contrary, it will assist the patient to respond more readily to it.—I am, etc.,

Shere. HARRY EDWARDS,
President, National Federation of Spiritual Healers.

SIR,—Dr. W. Melville Christie (May 28, p. 1652) tells us that the process of healing is no more a spiritual matter than is the digestion of food, but that both are accomplished by the same intelligence which controls the activities of the body cells. One would like to ask him his views of the nature of this "intelligence." Some would have difficulty in discussing it without mentioning the spiritual realm.

The primitive peoples whose attitude he believes to be outdated have a clear realization of their utter dependence on this mysterious "intelligence." It is our loss that so often education blinds us to the recognition of the fact that we are just as dependent as they are. We have, however, one great advantage over our primitive ancestors: the Christian religion has been given to us. Those who study it will find an entirely rational and satisfying teaching about this controlling "intelligence"; furthermore, they will realize why Christians believe that the "intelligence"—they call it "God"—is in fact influenced by the spiritual communion known as prayer.—I am, etc.,

Welford, Rugby. G. R. M. SICHEL.

SIR,—The remarks of Dr. W. Melville Christie (May 28, p. 1652) concerning healing really cannot pass without comment. He implies that healing may only be accomplished in accordance with the laws of nature by purely environmental and directive means. The gross materialism of this approach is more consistent with the primitive mentality which your correspondent attributes to any who claim that healing is a spiritual matter and that certain individuals may possess special healing powers.

The truth of the matter is that man is a spiritual creature, created by God, with a body, mind, and spirit. Each aspect of man's being is of equal importance and may have a remarkable influence on the other aspects. The effect of the mind on the body is widely accepted and the reverse is also recognized to be true in most upsets of bodily function. What is not so generally realized is that the spiritual condition of an individual may have a most profound effect upon his mind and his body. No person is really healthy unless he has a healthy body, mind, and spirit working in complete harmony with each other. Healing, therefore, should aim at the restoration of the wholeness of this unity, and any attempt to exclude one of these aspects of man's personality from an approach to healing is doomed to failure or at the most only partial success.

Convinced and enlightened Christians believe that God is at work in and through orthodox medicine, which, as your correspondent suggests, seeks to direct and assist the natural laws to man's benefit. This, however, is not God's only way

of bringing about the wholeness of man. He uses the age-old sacrament of anointing, which dates back to Apostolic times, and also to certain people He bestows a definite gift of healing or charisma. There is nothing unscientific about any of these methods of healing—they are merely examples of the divinely planned interaction of the aspects of man's personality. Spiritual things therefore, far from having nothing to do with healing, hold an equal place with medicine and psychiatry in promoting the wholeness of man's nature.

As the body and mind are the provinces of the physician, surgeon, and psychiatrist, so the spirit is the province of the priest. It is the hospital chaplain, therefore, who should direct the spiritual welfare of patients in hospital, and any spiritual ministrations should only be carried out with his knowledge and approval. Much of the present controversy about admission of "healers" to hospital would have been prevented if the chaplain, as a member of the hospital staff, had been approached first. Mutual co-operation between medical staff and clergy would go a long way to a more integrated and sane attitude to the work of healing.—I am, etc.,

Birmingham, 20. K. E. LUCKMAN.

SIR,—The admission of spiritual healers in British hospitals raises a matter of great concern not only in Britain but throughout the Commonwealth, which receives most of its inspiration and guidance from Britain.

The progress of medicine on scientific lines has not always been very easy; in the past it had to face witch medicines, black magic, miracles, and the rest, and there are "spirit operators." No wonder if in the future it may have to face some other subtle forms. It seems the cunning of men in devising methods of paranormal healing will never be exhausted. It is a pity that these benevolent men with a special healing cult were not born in those "good old days" when their skill would have been better appreciated.

Now the Consultants and Specialists Committee has expressed its view on the subject (*Supplement*, May 7, p. 266) we hope the Council of the B.M.A. will soon make its view known to the profession and the public in unambiguous terms.—I am, etc.,

M. A. HOSSAIN.

The Royal London Homoeopathic Hospital, London, W.C.1.

Smoking and Personality

SIR,—The paper of Professor H. J. Eysenck and his co-workers (May 14, p. 1456) again points up the highly complex and varied nature of the possible determinants of lung cancer. Here I would like to add to a list of neglected predisposing factors the presence of lymph-adenogenous perforative bronchial scars in about 25% of the adult population in both the United States and Europe.[1]

In postulating that a positive relationship exists between these scars, cigarette-smoking, and bronchial carcinoma, one may point out the following: lymphadenogenous perforative scars are often found in major bronchi; material from cigarette-smoke tends to accumulate in respiratory epithelium depleted of cilia or deprived of their protective action,[2] thus causing the scars to be exposed to greater concentrations of carcinogens; cigarette smoking is associated with bronchial changes ranging from basal-cell hyperplasia to squamous metaplasia[3-4]; and carcinomatous changes are sometimes incidentally found in otherwise scarred or structurally altered bronchi. Perforative bronchial scars may thus be related to bronchial carcinoma by a predisposition to metaplasia; by being more exposed to, and possibly also more susceptible to, the malignant effects of carcinogens than normal bronchial epithelium; and by determining the sites where certain types of bronchial carcinoma may originate. One may add that as these scars appear to be caused principally by perforations of tuberculous lymph nodes into bronchi—a not uncommon event during any phase of pulmonary tuberculosis—it is possible that there is currently an increased incidence of these scars in adults because of the declining mortality of populations exposed to, or suffering from, clinical and subclinical pulmonary tuberculosis.[5]—I am, etc.,

Albert Einstein College of Medicine, Yeshiva University, New York. HANUS J. GROSZ.

REFERENCES

1 Grosz, H. J., *Dis. Chest*, 1959, **36**, 514.
2 Hilding, A. C., *Ann. Otol. (St. Louis)*, 1956, **65**, 116.
3 Auerbach, O., Gere, J. B., Forman, J. B., Petrick, T. G., Smolin, H. J., Muehsam, G. E., Kassouny, D. Y., and Stout, A. P., *New Engl. J. Med.*, 1957, **256**, 97.
4 Chang, S. C., *Cancer*, 1957, **10**, 1246.
5 Professor Philip Schwartz. Personal communication.

Addiction to Hypnotics

SIR,—Dr. I. Pierce James (May 14, p. 1504) refers to the *Interim Report of the Interdepartmental Committee on Drug Addiction* (1960, H.M.S.O.), according to which cases of habituation to carbromal and bromvaletone were "numerically very few, but individually serious," and he comments that "whilst this may be so in England, there is reason to believe that it is not universally true." The cases of carbromal habituation which Dr. James reports from Australia were "largely confined to . . . neurotic individuals of potentially drug-dependent personality," most of whom had also taken alcohol or other drugs to excess. Amongst this latter type of patient, however, habituation to carbromal preparations seems also to be a not uncommon occurrence also in this country.[1-3] Amongst this small "habituation-prone" segment of the population carbromal preparations and the stimulant phenmetrazine were the most frequently abused drugs. Both have now been put on (Part I of) the Poisons List,[4] and it is to be hoped that this step will markedly decrease their abuse, just as it did a few years ago in the case of methylpentynol. This type of personality seems to be unable to handle any sedative or stimulating drug in moderation, though so far the relative absence of reports of habituation to the phenothiazines seems noteworthy.

Of some interest may be the case of an alcoholic neurotic who had been previously habituated to barbiturates, carbromal, amphetamines, and phenmetrazine; chlorpromazine was prescribed (25 mg. t.d.s.) for him during a state of great tension, but after taking about ten 25-mg. tablets on the first day he threw the rest of the chlorpromazine tablets away rather disgustedly, as they obviously had failed to provide him with what he was looking for. However, writing from Australia a year ago on the frequency of addiction to unrestricted drugs, such as carbromal, Drs. Minogue and Kyneur[5] remarked that "even the new tranquillizers, such as chlorpromazine . . . become drugs of addiction."

Dr. James states that, in such cases of drug habituation, "the seriousness from a prognostic point of view stems more from the patient's personality defect than from the particular drug of habituation." Long-term prognosis seems to rest mainly on underlying

personality, attitudes, etc. Treatment, therefore, has to be concerned with more than mere withdrawal of the drug which happened to be the "offender" on this particular occasion. Otherwise the hope that the patient will not find an as yet unrestricted substitute drug will, as a rule, sooner or later prove futile.—I am, etc.,

St. Bernard's Hospital, Southall, Middlesex. M. M. GLATT.

REFERENCES

1 Seager, C. P., and Foster, A. R., *Brit. med. J.*, 1958, **2**, 950.
2 Copas, D. E., Kay, W. W., and Longman, V. H., *Lancet*, 1959, **1**, 703.
3 Glatt, M. M., ibid., 1959, **1**, 887.
4 Ibid., 1960, **1**, 1139.
5 Minogue, S. J., and Kyneur, F. J., *Brit. med. J.*, 1959, **1**, 238.

"Honour a Physician"

SIR,—I have been infinitely depressed at reading your reviewer's castigation of Philip Auld's little masterpiece, *Honour a Physician* (May 28, p. 1625). As a market-town G.P., complete with cottage hospital, I ought to manage medical life on a higher plane than Auld's hero from the industrial north, but I can honestly claim personal experience of most of the predicaments in which he finds himself. So far from Auld's book being a catharsis, it is a very adequate commentary on the way in which a sizable minority use the G.P. part of the Health Service. I think he must have found his niche in industry, or he would never have had time to write the book. And as a conscientious G.P. being ground between the N.H.S. millstones, I cannot follow him too soon.

The book should be made required reading for every member of every committee that has to do with the running of the general medical services. It should also be a textbook in preclinical medical schools. Finally, it should be given to every Member of Parliament immediately upon election. Then we might get the right sort of person in general practice, if it is possible to design a sufficiently submissive donkey with the required intelligence.

Philip Auld is a pseudonym. Lest my patients identify me, may I sign myself

"UNHONOURED."

Postgraduate Study for G.P.s

SIR,—I read with great pleasure of the Nuffield Foundation's recently announced grant for general-practitioner postgraduate study in periods of six months (May 14, pp. 1491 and 1516). The greatest handicap to a general practitioner in regard to postgraduate study is lack of time. The opportunity to set aside for a period the exacting day-to-day matters of practice and to devote himself exclusively to postgraduate study will give a great boost to his morale and to the quality of his work.

May I, however, make one small criticism? Such study as envisaged, which is not concerned with the nature and management of general practice, could surely be carried out more effectively at a centre within the British Isles, where the student would be already familiar with hospital and university procedure and layout, and where the question of accommodation for self, wife, and children on holiday would be more straightforward, and so where the student would be able to apply himself more completely to the primary object of study. From the point of view of clinical or research material, there is a vast supply available in this country with a more pertinent application to general practice here, before one would wish to add the doubtful advantage of an international flavour. Furthermore, the age group aimed at, with practices based in many cases on their homes, and with the ties of children and school, would probably be reluctant to go to Canada, the U.S.A., etc., but would be able and most willing to go to the centres in this country. Possibly some of the most representative and most suitable general practitioners would lose the opportunity in this way.

There is a further extension of this conception which perhaps deserves thought. In essence the Nuffield Foundation Grant provides awards for suitable practitioners, and at the same time stimulates a better quality of work—both of which considerations constitute the purpose of the much debated general-practitioner merit award scheme. Could not a proportion of the £500,000 be devoted to this type of plan? May I conclude by expressing appreciation of the generosity of the Nuffield Foundation, and of the initiative of the College of General Practitioners.—I am, etc.,

Ash Vale, near Aldershot. S. G. A. BARTLETT.

Diploma in Dermatology

SIR,—May I commence by complimenting Dr. H. R. Vickers on his most interesting and enjoyable Watson Smith Lecture (March 26, p. 893)? He has very rightly emphasized the importance of a sound training in clinical medicine, with which dermatological conditions so frequently overlap and are an integral part. He likewise emphasizes the importance of dermatology in general medicine as a whole. I would point out, however, that his opinion that "it would be a retrograde step to introduce a diploma in dermatology" is not the prevailing opinion throughout the world. This will be seen from the fact that at the International Congress in Dermatology in Stockholm in 1957, when the teaching of dermatology was under consideration, the representatives of every country present, *except one only*, were in favour of "proof of knowledge of dermatology" by examination.

How else can it be ascertained that a person commencing to practise dermatology (or who has been practising dermatology for several years) has a proper knowledge of the subject fitting him to deal with all aspects? With the exception of the F.R.C.P. Edinburgh, where a man can "major" in dermatology, I know of no other fellowship qualification in the British Commonwealth in which a reasonable knowledge of dermatology is required. To be properly qualified to practise dermatology, an individual should possess proof of acquired knowledge by examination (as in the diploma in dermatological medicine at the University of Sydney) of (1) dermatology and its associated ancillary subjects—for example, embryology, physiology, histopathology, mycology, etc., (2) radiotherapy, including the clinical uses of *x* rays, radium, and radioactive isotopes, the associated physics and electrotechnology, and (3) a reasonably good knowledge of general medicine, particularly in the overlapping fields.

May I say here, that I am also very much in favour of a dermatologist becoming an F.R.C.P., or F.R.A.C.P. as well, if he can afford to do both. The point I wish to emphasize is that a well-qualified dermatologist must be "essentially a good dermatologist with a special

interest and grounding in general medicine," not the other way round as advocated by Dr. Vickers, or he could not be a "top-notch" dermatologist. I have yet to meet the man who, having obtained a fellowship and a diploma in dermatology, can keep right up to date in all aspects of both and run a busy practice at the same time. Hence dermatology must take precedence, but not at the expense of general medicine to too great a degree. With the exception of the above aspect of the association of dermatology with general medicine, I agree thoroughly with everything else Dr. Vickers said.—I am, etc.,

Sydney. JOHN C. BELISARIO.

Anaemia due to Phenobarbitone

SIR,—In the article entitled "Megaloblastic Anaemia Due to Phenobarbitone," by Drs. I. Chanarin, J. Laidlaw, Lavinia W. Loughridge, and D. L. Mollin (April 9, p. 1099) the statement is made, "megaloblastic anaemia due to this very widely used barbiturate has not been recorded."

Although I have been able to find no case of this type recorded in detail, mention has been made,[1] though little data supplied, of "another case" (of megaloblastic anaemia) "attributable to phenobarbitone only, with a haemoglobin of 4.6 g. per 100 ml., in which the marrow resembled that of pernicious anaemia." A. L. Sherwin and co-workers,[2] in a paper entitled "Megaloblastic Anaemia Associated with Phenobarbital Therapy," made reference to the preceding case as follows: "Only one previous case has been reported of megaloblastic anaemia associated with the administration of phenobarbital alone."—I am, etc.,

Long Beach, California. GEORGE X. TRIMBLE.

REFERENCES

[1] Dawson, D. W., and Johnson, J., *Brit. med. J.*, 1958, **1**, 397.
[2] Sherwin, A. L., Wait, R. H., and Cooper, B. A., *Canad. med. Ass. J.*, 1960, **82**, 368.

Spondylarthritis

SIR,—I write to correct an error occurring in your report on the Joint Meeting of the British and Dutch Orthopaedic Surgeons (May 28, p. 1647). In your report of the paper I read entitled "The Stiff Back in Children," the term spondylolisthesis is printed instead of the term spondylarthritis. Spondylarthritis is a name used first by Saenger[1] and again by me to describe the condition of acute pyogenic infection of the spine. Spondylolisthesis is, of course, a completely different entity and was not mentioned in my paper.—I am, etc.,

Royal Hospital for Sick Children, Glasgow, C.3. N. J. BLOCKEY.

REFERENCE

[1] Saenger, E. L., *Amer. J. Roentgenol.*, 1950, **64**, 20.

*** We regret the mistake.—ED., *B.M.J.*

Osteoarthritis of the Hip

SIR,—I would like to comment on the letter by Dr. W. K. Dunscombe (May 7, p. 1427) and on that by Dr. J. E. Swinburne-Jones (May 21, p. 1564).

Firstly I would like to comment on Dr. Dunscombe's letter. I would be interested to know whether the disabilities about which he complains post-operatively existed pre-operatively, because I find that most of the patients I see with osteoarthritis of the hip cannot carry out tying their shoes or putting on their stockings, etc. Also, in my view, there is no need to search for a universal operative procedure for the unilateral osteoarthritic hip; it already exists and lies in a sound arthrodesis. Most patients can post-operatively put on their socks; they just have to learn another way of doing it. They obviously cannot, except in the younger age group, bend forward, but by flexing up their knees there is no great difficulty. I feel that if Dr. Dunscombe balances out the loss of pre-operative disabilities, about which he complained, particularly pain, against any slight loss he might have incurred post-operatively, he should be quite happy.

With regard to Dr. Swinburne-Jones's letter, I was quite appalled to read it. I see a fair number of osteoarthritic hips occurring mainly over the age of 65, and some of them over 70. Post-operatively they are up on their feet after three weeks, walking, and the majority of them end up with one stick, going home four to five weeks after operation. A very large proportion, 50%, on attending out-patients do not use a stick at all. As Mr. John Charnley rightly points out (May 21, p. 1564), this should be an operation in which the services of the physiotherapists are practically eliminated. The patients should not lose knee movement but, if anything, regain what they have lost, if necessary helped by a manipulation in the anaesthetic room pre-operatively.

The picture that Dr. Swinburne-Jones conjures up of an individual tottering about on two sticks or elbow crutches is a pathetic one and should not be taken as an invariable result of operation. I can assure him that, on the whole, the results are excellent provided the patients will remember and compare what they have gone through post-operatively as against what they suffered pre-operatively, particularly with regard to pain. The operation was never intended to compete with a normal hip.—I am, etc.,

Hove, Sussex. W. LAURENCE.

SIR,—Mr. J. Charnley (May 21, p. 1564) has produced the wrong prosthesis. I said nothing for or against physiotherapy, and his panegyric makes it depressingly evident that he is unaware how profoundly the mechanics of a fixed hip modify the movements of ordinary, i.e., post-hospital, everyday life.

I have been left with a knee that can be flexed to the extent he suggests and a bony ankylosis, so that now eight years after the operation the chief aim has undoubtedly been achieved, for which I am extremely grateful to the eminent orthopaedic surgeon who operated on me. This does not, however, alter the point which I had hoped was plain in my letter, that a fixed hip must have a considerable effect on the patient's daily life however excellent the operative craftsmanship, and that therefore the less experienced operators especially should be fully aware of the disabilities likely to occur subsequently. Mr. Charnley's athletic arthrodetics may all be Olympic gold medallists, but can these heroes cut their toenails? Perhaps they use a *digital* computer!

It should be emphasized that reliance on what can be called colloquially "gadgets" is fatal, as it is precisely when the patient is away from home and when he perhaps needs them most that they are lacking. However, *pace* Dr. J. E. Swinburne-Jones (p. 1564), the drill for putting on a sock is reasonably simple provided the knee can be flexed to over a right-angle and that the spine is reasonably mobile.—I am, etc.,

Penzance. W. K. DUNSCOMBE.

Shoes for Children

SIR,—In the letter which followed Dr. Margaret Emslie's valuable statement on "Shoes for Children" (April 2, p. 1052) it was interesting to note Dr. Catherine Swanston's suggestion (p. 1053) that "a deformed gene" might be partly responsible. Dr. Emslie's view that the terminal phalanx of the great toe displaced towards the centre of the foot is "the first and irrecoverable stage in the creation of a hallux valgus" may be modified by a published series of studies[1] of adult and *foetal* great toes in which it was noted that the *diaphysis* of the terminal phalanx is not usually set at right angles to the plane of the epiphysis but *normally* deviates towards the outer side of the foot. Since coming to West Africa I have repeatedly observed this diaphyseal angulation in radiographs of feet which have never been shod.—I am, etc.,

Nixon Memorial Hospital, Segbwema, Sierra Leone. J. L. WILKINSON.

REFERENCE

[1] Wilkinson, J. L., *J. Anat. (Lond.)*, 1954, **88**, 537.

SIR,—Dr. Catharine Hollman (March 5, p. 719), Dr. Catherine Swanston (April 2, p. 1053), and all the rest are quite wrong, and only the shoe-manufacturers, with Mr. J. Anthony Clark (March 12, p. 803) as their spokesman, hold the real truth about the human foot. To their credit they have shown no mean selfishness about this secret in keeping it to themselves. On the contrary they divulge it openly in their shop windows for all who have eyes to see, but nobody believes them. What they are telling us as clearly as they can, but what our profession refuses obstinately to believe, is that there are *two forms of the human foot*.

First they have discovered the primitive form which, as it exists up to the age of about 13, may be called the pre-puberty type. This type of foot is broad in front with toes which can move independently. The observant shoe manufacturers make shoes to conform to this foot. They do it well. The toes have plenty of room to wriggle about in, and there are no corns.

Secondly, they observed something which our profession has remained blind to—namely, that after 13 the human foot undergoes a startling modification almost overnight. This may be called the post-puberty foot. The middle toe is still directed straight forward, but the other four toes rapidly grow towards it, even eventually displacing it upwards or downwards, and finally forming a coalescent toe-mass in the shape of a triangle, of which the middle toe is the apex, the heads of the metatarsals the base, and the two sides are formed by the external borders of the adherent toes. I hope I make myself clear, but it is not easy without the use of diagrams. Thus is formed the normal pointed adult foot, and the shoe manufacturer, aware of this simple developmental fact, obligingly and becomingly furnishes us with the pointed shoes appropriate to this type of foot. No one looking in a shoe-shop window with eyes in his head can fail to distinguish these two distinct and separate types of human foot. Only a wilful obstinacy can deny it.

Sir, I should not be taking up your valuable space labouring this banal and self-evident fact, were it not to emphasize that there are certain people, unknown in number (I, alas, am one of them), who do not conform to this regular development of their feet. We are what one may call aberrant types. Our toes have never behaved like other people's toes and sought the middle line of the foot after puberty. They have retained the infantile form (no doubt due to some childhood fixation) and have not coalesced, but remained separate and still seek to wriggle individually in the old childish way. We have long outgrown the pre-puberty shoe, but from our inability to develop the normal adult toe triangle our feet simply cannot be stuffed into the ordinary pointed post-puberty shoe. The point of this letter is to work upon Mr. J. Anthony Clark's feelings of compassion so that he may influence his firm to make for us foot monstrosities some adult-size shoes of the infantile type. Let him picture us as with aching hearts and feet we longingly search his shop windows—in vain. Will he not have pity on us? We may be few or many: it may be our glands which have retarded the development of our feet, but we cannot help it and our sufferings are great. We confess with sorrow that our pheet are phat, but why should we not be kumphy as the children are? We do so long to wauk as eesi as they do.—I am, etc.,

London, W.1. A. J. HAWES.

*** This correspondence is now closed.—ED., *B.M.J.*

Therapeutic Abortion

SIR,—While I do not wish to enter into the controversial question of psychiatric indications for therapeutic abortion, on which Professor T. N. A. Jeffcoate writes (February 27, p. 581), I should like to make a few comments.

The requests for abortion received by general practitioners are, I am sure, far more than can be indicated by any kind of statistics, for the reason that so many women have a fleeting—often unexpressed, or unverbalized—desire to do away with the foetus and then think or do no more about it. Still others may approach their family doctor and on meeting a refusal just accept the inevitable. In the cases where the desire to have an abortion persists, and where, nevertheless, we cannot oblige, surely instead of just turning these patients away we must realize that they are sick persons and persuade them to see a medical or a psychiatric social worker or a psychiatrist. This applies more so to cases that go to full term. If this is not possible or is omitted, after confinement they should be persuaded to see these workers to ensure that the mothers are enabled to come to terms with their feelings and that they do not go through life rejecting children they never wanted—such unwanted children are not likely to grow up into willing and accepting parents.

In the controversy over legality and medical ethics we seem to lose sight of the fact that at present, except for admonitions, sermonizings, and other expressions of self-righteous indignation, precious little is done to help these mothers accept their femininity and motherhood. Most of these women came to the doctor as a last resort, and our attitude of rejecting both the women and their feelings, apart from often indicating a lack of humanity, aggravates the problem, leading in some cases to resort to desperate measures.—I am, etc.,

Bombay, 1. D. M. BASSA.

Toxicity of Asbestos

SIR,—The majority of our pathological terms are derived from Greek, but the chain of derivation is sometimes long and slender; in no case more so than in that of the terms "toxin," "toxicity," and "toxicology."

The Greek word is "Τοξον" (toxon), meaning "a bow," the weapon from which "arrows" or "bolts" are shot. The word for "arrow" or "bolt" is

"Τοξευμα" (toxeuma), which inflicts the "toxic" injury. It might therefore be etymologically more accurate if we spoke of substances being "toxeumatic" rather than "toxic," just as it would certainly be more correct to speak of "pneumonokoniosis" rather than "pneumoconiosis." But in the case of asbestos dust the derivation is singularly apt, because it is the point of the asbestos fragment that is "toxic," just like the point of the arrow. Consequently the fragment of asbestos accumulates a ball of organic material containing iron from the blood—haemoglobins of the tissues it has "toxed"—at its ends. When its surface activities have done their worst, the asbestos body remains—an inert alien—and is coughed out with the sputum.

This limited "toxicity" of the broken asbestos fibre is dependent upon its peculiar atomic lattice-structure. Similarly, in the case of mica and talc the "toxicity" is limited to the broken edges of the platelets. But in the case of freshly produced dry dust of pure silica the whole surface of the fragment is "toxic." Hence it follows that silica dust is so much more "toxic" than is that of silicates.

American and French workers have accepted these facts long ago. But in Britain, particularly—dare I say in "Ancient Britain"?—the idea still prevails that a substance before it can become "toxic" must enter into "solution," and years of effort have been spent in trying to co-relate the relative solubilities of dusts with their "toxic" effects, just as if the work of Laue and the Braggs, father and son, and of the brilliant Oxford lady who now adorns the Royal Society, had not demonstrated the importance of atomic lattice-structure in the matter of the chemical activity of solids, as testified to every household which uses a "permutit" water-softener. Apparently the Greeks knew better, and found a suitable word for it.—I am, etc.,

Bognor Regis. PATRICK HEFFERNAN.

Nocturnal Dogs, Piscatory Cats, Eton College, and Alcohol

SIR,—My paper—"Clinical Sense" (April 2, p. 985)—referred to human error in observation. Correspondents who have written to you about my paper since then have emphasized this very ably. Dr. Valerie Box (May 7, p. 1433) got the title of my paper wrong, the title of Conan Doyle's story inaccurate, and the quotation from the story incomplete. Dr. R. Christopher Howard (May 21, p. 1573) referred to the wrong poem (how odd to confuse drowned cats with a distant prospect of Eton College) and even the right poem contains the wrong meaning; my mention of gold glittering among dross was not a quotation of any kind. Dr. John Miller (April 16, p. 1211) was more accurate, but forgot that alcohol is an anaesthetic; Keats recognized this when he called, "Oh, for a beaker full . . .," explaining that he wished to take enough to "leave the world unseen."

The impervious armour of extensive learning is not possessed by all epistolatory gladiators; but at least they can take the trouble to acquire a temporary outfit by visiting the cultural equivalent of Moss Bros.—the Public Reference Library. Among quotations they might find there, I commend to them the following: "Read not to contradict and confute, nor to believe and take for granted, nor to find talk and discourse, but to weigh and consider."—I am, etc.,

London, W.1. RICHARD ASHER.

Otolaryngology

SIR,—I would like to send to you and to the editorial board of the *B.M.J.* a note of appreciation on the adoption of Otolaryngology instead of "E.N.T., etc.," as a heading for "Posts Vacant" in the O.R.L. specialty in your advertisement columns. The official recognition now given by a journal of the standing of the *B.M.J.* to the naming of the specialty in this country should receive a general welcome, as it brings the title into line with its present status and with international practice.—I am, etc.,

Birmingham, 15. W. STIRK ADAMS.

The Great Hall

SIR,—The Association must have been using its Great Hall for more than thirty years. The interior ceiling must be one of the ugliest of any building of a similar size and distinction in London. Could we please ask the Council to give serious consideration to completing its construction at last?—I am, etc.,

London, W.13. R. E. W. OLIVER.

POINTS FROM LETTERS

Smoking and Personality

Dr. LENNOX JOHNSTON (Wallasey, Cheshire) writes: I was interested to note that the investigation into the validity of Fisher's hypothesis by Professor H. J. Eysenck and others (May 14, p. 1456) was sponsored by the Tobacco Manufacturers' Standing Committee, interested because they, more than anyone else, seem to be fully aware of the *real* reason why people at all events *start* to smoke. "Smoking is spread by smokers"—by their example and persuasion. There are over 30 million smokers in this country and therefore over 30 million living advertisements for tobacco. Despite this, the tobacco manufacturers are most lavish advertisers (or persuaders) in this country.

Speech Therapy and Child Guidance

Miss PATRICIA GRADY and Miss HELEN ALDRIDGE (Child Guidance Centre, Nottingham) write: We are speech therapists whose headquarters is a child-guidance clinic, and who enjoy the full co-operation of medical and child-guidance staff. . . . It is usual, under these conditions, for the child-guidance staff and speech therapists to work under their own senior or head of department, and for the senior or principal school medical officer to supervise the working of the whole. Patients are quickly and easily referred to different members of the clinic for assessment of speech, psychiatric, or educational difficulties, and intelligence testing. The various records and case histories are available to all. Conferences about patients are arranged as necessary, but rarely do patients receive speech therapy while attending for psychotherapy. . . . Thus, any child whose home background is unstable, or who is presenting emotional problems with which the speech therapist is not qualified to deal, is promptly referred to the appropriate member of the child-guidance team—a course of action which, we trust, is followed by all responsible speech therapists.

Side-effects of Aspirin

Dr. N. HARRIS (Sutton Coldfield, Birmingham) writes: I have noted with interest the two letters (May 7, pp. 1425–6) in which reference is made to certain possible effects of long-continued and heavy aspirin therapy. For some years I have employed a proprietary compound, in tablet form, containing, in addition to 5 gr. (0.32 g.) of soluble aspirin per tablet, ¼ mg. synthetic vitamin K and 20 mg. ascorbic acid. These two latter quantities are claimed to be in the exact proportions which are needed to counteract the inactivation of these vitamins by aspirin. . . . It occurs to me that this product should also be of value in cases in which concurrent anticoagulant and aspirin therapy may appear desirable.

Obituary

Sir HENRY TIDY, K.B.E., M.D., F.R.C.P.

The world of clinical medicine and also of military medicine has lost a distinguished figure by the death on June 3 of Sir Henry Tidy, Extra Physician to the Queen, and consulting physician to St. Thomas's Hospital and the Royal Military Hospital, Millbank.

Thousands of medical men, not only in Britain but in the United States and Canada and various Allied countries on the Continent who served in the second world war, will recall Tidy's chairmanship of the twenty-four Inter-Allied Medical Conferences which were held at the house of the Royal Society of Medicine from 1942 to 1945. More than two hundred principal contributions were made on every aspect of war medicine, from the conduct of a continental campaign to personal experiences and unusual episodes. It was Tidy who conceived the programmes and devoted his time and energy unsparingly to ensuring the success of the meetings. He presided over the informal dinners which followed, when the proceedings sometimes took place to the accompaniment of air raids, but it took more than a bomb or two on the W.1 district to upset Tidy's imperturbability in the chair, and his zeal and enthusiasm infected successive audiences. The conferences were held under strict security, but after the war was over Tidy did further good service by acting as honorary editor of a volume recording the proceedings. What did not lend itself to such a record was the new fellowship which was generated between medical men of different countries and ranks and branches of medicine.

Henry Letheby Tidy was born, the son of a doctor, on October 27, 1877. He was educated at Winchester and New College, Oxford, and received his medical training at the London Hospital, with some postgraduate study in Freiburg and Berlin. At the London he won scholarships in medicine and pathology, and later he was awarded the Gillson research scholarship by the Society of Apothecaries. Graduating B.M., B.Ch. in 1905, he held the post of demonstrator of clinical pathology at the London, and thereafter became physician to the Poplar Hospital and the Royal Northern Hospital, but his main work in the hospital field followed his election to the staff of St. Thomas's, which he served as physician and consulting physician until the close of his life. In 1938 he was made dean of the St. Thomas's medical school. He had taken the M.R.C.P. in 1908, was elected to the Fellowship in 1911, and in the same year he proceeded D.M.

In the first world war Tidy served with the R.A.M.C. and attained the rank of major. He carried out much useful work and observation among the troops in France. One of his earliest publications (in the "Special Reports" series of the Medical Research Committee) was of an epidemic occurring amongst them caused by *B. aertrycke*. His interest in military medicine, particularly from the epidemiological point of view, and also from the point of view of standards of physical fitness, continued during the inter-war period. At the outbreak of the second world war he was appointed consultant physician to the Army at home, with the rank of colonel. He relinquished his commission in 1942, and was granted the honorary rank of major-general. For many years he was consulting physician to the Queen Alexandra Military Hospital, Millbank, and from 1946 to 1951 he was visiting professor at the University of Cairo.

In addition to his clinical aptitude he had administrative gifts of a high order. He held various offices, including those of examiner, councillor, registrar, and censor in the Royal College of Physicians, and he was representative of the College on the General Medical Council from 1929 to 1944. During the last five years of his membership of that body he served as its treasurer. He was at various times examiner in medicine to the Universities of Glasgow, Manchester, Durham, and Sheffield, and the Queen's University, Belfast. For some years he was honorary secretary to the Royal Society of Medicine, and he was its president in 1942. He was also treasurer and later president of the Association of Physicians of Great Britain, of the Gastro-Enterological Society, and of the Royal Medical Benevolent Fund. At the Annual Meeting of the British Medical Association in Glasgow in 1922 he acted as honorary secretary of the Section of Medicine, and he was vice-president of the Section at the meeting in Cardiff in 1928. He was also a member of the Medical Planning Commission set up in 1940.

Sir Henry Tidy was a busy editor. His famous *Synopsis of Medicine* ran through many editions, and he was editor of an *Index of Symptomatology*, published in 1928. He was also co-editor of the *Medical Annual* from 1934 onwards for many years. Although his manner conveyed a certain shyness or diffidence, he was a frequent participant in discussions in medical societies and a correspondent of the medical journals. Every aspect of internal medicine appeared to interest him, and the experience on which he could draw was very wide. He had an eye also for the unusual case as well as a love for the byways of medical history, resulting in acute and sometimes humorous observations or discoveries which he would recount in medical gatherings. His published descriptions of glandular fever in this and other journals threw much new light on this infection, which he made the subject of his Lumleian lectures to the Royal College of Physicians in 1934. He was also an authority on Banti's disease.

Sir Henry Tidy was held in high esteem by all who knew him for his sound judgment and his invariable kindness to colleagues and juniors. He received many distinctions. He was knighted in 1943. In 1947 the President of the United States conferred on him the Commandership of the Legion of Merit, U.S.A., and in the same year he was given the Order of the White Lion (Czechoslovakia), and was made a Grand Officer of the Order of Orange-Nassau (Netherlands). In 1948 the Hon.LL.D. of Queen's University, Belfast, was conferred upon him. In 1936 he became physician-in-ordinary to the household of the Duke and Duchess of York, and after holding the appointment of Extra Physician to King George VI he became Extra Physician to the Queen in 1952.

He married Elizabeth Catherine, daughter of Sir William Ramsay, the famous chemist, and had two sons, one of whom is a doctor, and one daughter.

H. G.-H. writes: Harry Tidy—as he was affectionately known to a wide circle of friends—will be deeply mourned by everyone who came into intimate contact with him, for the very essence of the man was that he was always out to help. He could not have had an enemy in the world. I can speak with appreciation and gratitude of his many qualities, for I had the good fortune to be his junior on a firm at St. Thomas's for many years, until, in fact, he retired from the teaching staff in 1938. But so highly was he thought of that he was asked by his colleagues to continue in the appointment of dean.

I think it was his essential kindliness and loyalty—to all the things that matter—that so endeared him to the people he had to work with: the fact that he was so distinguished in so many fields was no bar to their approaching him as personal and privileged friends. Yet he was a patrician from the roots—a figure, and a figurehead when necessary, but a very actively functioning one (as can be judged from

the large number of committees, conferences, and societies for which he was asked to take the chair).

To the firm he was "the Old Man," a term signifying his colleagues' affection rather than his antiquity, for no one could have been younger in outlook or presided with more *joie de vivre* over the Athletics Club, which he did for many years, or one of the firm's parties. The latter were regular meetings, at his house or mine, designed to give members of the firm, past or present, an opportunity of keeping in touch with each other and with what was going on, particularly after they had ceased to take an active part in the work of the hospital. It was typical of him that he wanted to keep people together and to have the opportunity of helping them. The result was that he was *pater familias* to many generations of medical students and house officers in the pre-war decade. He was an admirable builder of team spirit.

His clinical teaching and outlook were much appreciated not only by his firm but by large troops of medical students who attended his rounds. His *Synopsis of Medicine* was especially designed in his early days to help the student compete with the examiner. Its popularity for many years testifies to the fact that this purpose had undoubtedly been achieved, but this synoptic book does not give any clue to Tidy's very common-sense views about the proper teaching of clinical medicine. He was all in favour of the clinical approach; the patient and his problem were to be studied as a whole, and he used to quote to his firm the old dictum that the objective of the best doctors should be to learn more and more about more and more, and not more and more about less and less—in fact not to become too specialized. He was essentially a general physician both in his teaching and in his practice.

With all these attributes and his great personal charm Harry Tidy could not help being popular. He took part in all the hospital activities which came his way. The annual staff and students' golf match was a good example: he was an ideal foursome partner—if he had a putt for the hole, his partner could guarantee that he would not have to hole one for the half. The same would apply to any other activity in which one was fortunate enough to be in partnership with him. I had that experience and am deeply grateful.

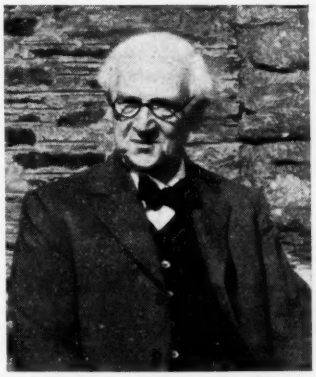
These few words do scant justice to the firm's leader for so many years, but they will at least let it be known what we all thought of him and how affectionately we shall treasure the memory of a great man and an outstanding physician.

CHARLES SINGER, M.A., M.D., D.Litt., Hon.D.Sc. F.R.C.P.

Dr. Charles Singer, emeritus professor of the history of medicine in the University of London, died in his sleep on June 10, at his home at "Kilmarth," Par, Cornwall, in his 84th year. He had long been regarded as the doyen of historians of medicine and science in this country, and indeed in the English-speaking world.

Charles Joseph Singer was born in Camberwell on November 2, 1876, the son of the Rev. Simeon Singer, a distinguished Hebrew scholar. He was educated at the City of London School under Edwin Abbott, and at the age of 17 he began the study of medicine at University College, London. After a year he transferred to the Faculty of Science, where he read zoology and botany. Gaining a scholarship to Magdalen College, Oxford, two years later, he read zoology at that university and graduated B.A. in 1899. He then continued his medical studies at St. Mary's Hospital, Paddington, and qualified M.R.C.S., L.R.C.P. in 1903. On the day on which he qualified he was appointed medical officer to an expedition which was departing on survey work in Abyssinia. As a result he collected many biological specimens and published a paper on some interesting clinical conditions. On his return Singer graduated B.M., B.Ch. at Oxford, held two resident posts, spent over a year in a post at the Government General Hospital at Singapore, and by 1909 he was medical registrar to the Cancer Hospital in Fulham Road and physician to the Dreadnought Seamen's Hospital. For the next five years, in addition to hospital and consulting practice, he carried out many laboratory investigations, some of which were presented at the International Medical Congress held in London in 1913.

Despite these promising studies it was already clear that Singer was deeply interested in the history of medicine. His fifth and sixth papers (1911) were historical, and by 1914 he had written twelve papers on historical subjects. One of these was delivered to the newly established Section of the History of Medicine of the Royal Society of Medicine, of which Osler was the first president and of which Singer was later to be president. In 1914 Osler offered Singer a studentship in "pathology" at Oxford, but most of his time was to be devoted to historical research. By his acceptance of this post Singer cast the die. After that date all his numerous papers were on historical subjects. Although the war stopped his work at Oxford, it did not seriously affect his studies. While holding a commission in the R.A.M.C. from 1914 until late 1918, he was able to do archaeological work at Malta, study Byzantine Greek at Salonika, and, with the assistance and co-operation of his devoted wife, to publish two books.



After the war Singer returned to Oxford, but in 1920 he received an invitation to lecture on the history of medicine at University College, London. He accepted, and in time he became very friendly with some of the distinguished professors, including Arthur Platt and H. E. Butler. In 1930 the University of London recognized Singer's merits by conferring on him the title of professor. But the office was honorary, and there was no official chair of the history of medicine in the university. Singer continued to adorn this office until 1942, when he retired with the title of professor emeritus. In the years between the wars Singer was several times vice-president or president of the Section of the History of Medicine at Annual Meetings of the B.M.A.

Another university which was dear to Singer's heart was the University of California at Berkeley. In 1929 and again in 1932 he acted as visiting professor at that university, and his lectures were very enthusiastically received.

In 1934 the Singers moved their residence from London to the house in Cornwall which is so well known to their many friends. While he continued to lecture at University College until the outbreak of the second world war, their time was more and more devoted to the relief of victims of Nazi oppression. He was actively associated with the foundation of the Society for the Protection of Science and Learning. These years therefore form a gap between his two great active periods.

A study of Singer's historical writings during the period up to the end of 1933 will show that his greatest original work was done between 1914 and 1925. These twelve years saw the publication of his very important papers delivered to the History Section of the Royal Society of Medicine in its formative years, and of several books. Of the latter seven are original and significant. The papers included his works on the early history of microscopy, on various aspects of the medical literature of the Dark Ages, on medieval and renaissance anatomy, and on some little-known Anglo-Saxon texts. They also included his classic paper of 1927

on "The Herbal in Antiquity," a subject on which he had first written in 1923. The important books show quite clearly the direction of his interests in later years. The first volume of his *Studies in the History and Method of Science* was a series of original essays by six scholars, including Singer himself. It was published in 1917, soon went out of print, and began to fetch fantastic prices at the sales until it was reprinted a few years ago. This work contained a very important study of Renaissance anatomy by Singer. It also contained the definitive version of his protracted study of the manuscripts dealing with the mystical visions of St. Hildegard of Bingen, which established migraine as a cause of such visions. Singer had published his first paper on this subject in 1913, and his own transcripts of the manuscripts had accompanied him for years on his travels. The second and final volume of the *Studies* was published in 1921. Of Singer's own two contributions, that on Greek biology broke new ground in a most detailed and inspiring manner. In the following year Singer produced a simplified version of his argument in his *Greek Biology and Greek Medicine*.

In 1920 Singer produced his first work on a subject which retained his interest right up to the time of his death. This was his *Early English Magic and Medicine*, originally delivered in the form of a lecture to the British Academy. In 1924 he reproduced and translated a 1491 edition of the Anatomy of Mundinus, and in 1925 he published the sumptuous *Fasciculo di Medicina Venice 1493*, a reproduction and translation of a slightly later variant of the same work. The early history of anatomy had been engaging his attention more and more, and in 1923–4 he had delivered at the Royal College of Physicians the FitzPatrick lectures on this subject. In 1925 these lectures were published as *The Evolution of Anatomy*, a book which broke new ground, contained much original material, and soon became a classic. In 1928 Singer republished some of the papers mentioned above in his *From Magic to Science. Essays on the Scientific Twilight*, a work which soon went out of print and recently has had a rebirth in the form of an American paper-back.

The year 1928 saw a change in Singer's interests in that it ushered in his period of general histories, each of which was widely used and quoted, and each of which was intended for, and reached, a much wider audience than his previous works. In 1928 he published his much-read *Short History of Medicine*. While he was in California in 1930 he worked and lectured on the history of botany and zoology, and these lectures led to his *Short History of Biology* (1931). Fifteen years ago Singer considered this to be his best book, but more recently his preference seemed to be for a later work on Vesalius. In 1950 he produced a revised second edition, and last year he published unaided a third edition still further revised.

The period from 1933 to 1945 was devoted mainly to occasional writings, some of which contain minor gems of wisdom. But during the early years of this period Singer's interests had veered towards early science, and he had been steadily working on his *Short History of Science to the Nineteenth Century*, which was published in 1941. During recent years he was active in revising and extending this work; and last year he published a much-enlarged edition with the title changed to *A Short History of Scientific Ideas*.

Singer's final period was really ushered in by the quater-centenary of the publication of the *Fabrica* of Vesalius (1543), which was celebrated in 1943. From his early years he had four continuing sources of interest: Galen, Vesalius, Anglo-Saxon medicine, and the early herbals. On the first two of these he had written virtually nothing of any importance. He now turned to work on Vesalius, and in 1946 he published, with Professor Chaim Rabin, *A Prelude to Modern Science*, which is a definitive critical edition of the *Tabulae Anatomicae Sex* of Vesalius.

Since about 1945 Singer had been engaged on a very specialized history of the alum trade, and the result was the beautiful volume, *The Earliest Chemical Industry* (1948). That completed, he returned to Anglo-Saxon studies, and worked with his friend the late Professor J. H. G. Grattan. This long task was completed in 1952 with the publication of *Anglo-Saxon Magic and Medicine*, which embodies a definitive critical text and translation of the *Lacnunga*. Concurrently he had been working intensively on the seventh book of the *Fabrica* of Vesalius, and in the same year he published *Vesalius on the Human Brain*, an annotated translation of that book. Singer had meanwhile been working steadily on his final contribution to the history of ancient medicine, an annotated translation of Galen's book, *On Anatomical Procedures*. This fine work was published in 1956.

It was characteristic of Singer that, as he grew older, his ideas and his literary ambitions broadened. By the time that he had completed his book on alum he felt convinced that a history of technology was badly wanted. He himself drew up the detailed plans for this co-operative work. On the vast scale on which he conceived it, it was obvious that he could not carry through the whole work single-handed, for he was by then, alas, in his 73rd year. However, by 1949 he had ensured the publication of the work, and had secured the assistance of associate editors, chief of whom was the late E. J. Holmyard. The project entailed much correspondence and editorial work. The first volume of *A History of Technology* was published in 1954, the second in 1956, the third in 1957, and the fourth and fifth volumes in 1958. The work was an immediate success.

In this tribute to this astonishing man mention has been made only of his more important works. His bibliography up to 1953 has been published elsewhere, and, with the additions since that date, it now runs to nearly five hundred publications. Yet the same threads may be seen running through the long span of years. At the time of his death he was closely associated with a scheme for reprinting Oswald Cockayne's *Leechdoms*, long a scarce book. He was again doing work on the history of anatomy. He had also been re-studying sporadically the early history of the herbal, with a view to publishing a much-enlarged edition of his early classic. But his death has prevented him from completing a project on which he had long been working—the history of the Medical School at University College Hospital.

From an early period Singer was prominent in the international field of the history of medicine and science. He was president of the Third International Congress of the History of Medicine (London, 1922), and president of the Second International Congress of the History of Science (London, 1931). He was actively associated with the foundation of the British Society for the History of Science, and he was its first president (1946–8). In 1947 he was elected president of the International Society for the History of Science. In 1954 he gave the Lloyd Roberts Lecture. In 1956 he was awarded the Osler Medal of Oxford University, and shortly afterwards he was the recipient of the George Sarton Medal of the American Society for the History of Science. He was an Honorary Fellow of Magdalen College, Oxford, and a Fellow of University College, London.

Singer retained his boyish enthusiasm right to the last. He was a brilliant conversationalist, a lively raconteur, and a large-hearted gentleman. His innumerable friends will remember with gratitude the hospitality so freely extended to them. He had an extensive correspondence with medical men, scientists, and historians all over the world. The respect with which he was regarded by the world of learning was shown by the presentation to him in 1953 of a co-operative work written in his honour. Though many of Singer's writings will live, the passing years will inevitably lessen the band of those who knew the man. Yet it may be that his inspiration will continue to thrive; his death is but a sleep and a forgetting.

In 1910 Singer married Dorothea Waley Cohen, whose work on alchemical and scientific manuscripts is well known. Throughout his married life he constantly acknowledged her assistance in the preparation of his works. He is survived by his widow, a son, and a daughter.—E. A. U.

A colleague writes: For a great many years Charles Singer kept in close contact with the *Journal* and helped three editors in succession to keep the lamp of medical history burning brightly in the occasional column under "Nova et Vetera." Many of his contributions were unsigned, but all bore the stamp of his learning. And in these articles he seemed to be less fettered than in his more formal papers and in his books. His style could become as light as a leaf, and he seemed to enjoy these excursions into journalism as an opportunity to escape for a while from the professorial chair. Along with his articles would come a letter full of a youthful zest in his comment on personalities in medicine: and for him the personalities of the remote past were as alive as those of his contemporaries. He never said no to a request for help, and it is sad to think that in the *B.M.J.* office we shall not again be able to enjoy seeing a letter written in his firm handwriting, full of youthful verve and wise counsel.

We are indebted to Sir ARTHUR MACNALTY for the following appreciation: Of late four eminent medical historians have left the world—George Sarton, Henry Sigerist, W. W. Francis, and John Fulton. Now we deplore the death of Charles Singer, the doyen of British medical historians.

Fifty years ago Charles Singer called on me at Brompton Hospital. He was then medical registrar to the neighbouring Cancer Hospital and investigating the composition of the gastric juice in certain diseases; and desired to extend his observations to cases of pulmonary tuberculosis. I obtained permission and facilities for him to do so. This early work was afterwards published in the *Quarterly Journal of Medicine*. The acquaintance thus begun ripened into a lifelong friendship.

Singer forsook clinical medicine to become the historian of science and medicine at Oxford. This was interrupted by military service in the R.A.M.C. in the first world war and resumed at its conclusion. In this sphere he received every encouragement from Sir William Osler, and at Osler's house I frequently met Singer and his devoted wife, who shared his interests and is herself a distinguished medical historian. Singer, by his investigations, published books, and papers, and teaching first at Oxford and then at University College, London, soon achieved world-wide reputation as a medical historian.

Singer had a generous and kind disposition. Many of his friends will remember his gifts of erudition, wit, and humour in conversation either at the Athenaeum Club or when they were guests at "Kilmarth," his house in Cornwall, where he and Mrs. Singer were always glad to welcome them. He was fertile in ideas, active in good causes, ready to help others, to right wrongs, or to redress grievances. In medical history his disciples will carry on the torch which he so brightly kindled. His end was peaceful, the close of a well-spent life.

W. S. PATTON, M.B., Ch.B.

Professor W. S. Patton, emeritus professor of entomology in the University of Liverpool, died in Bideford Hospital on May 24, after a fall in which he fractured a femur. He was 83 years of age.

Walter Scott Patton was born at Hyderabad, Sind, on October 7, 1876, the son of William Patton, J.P., of Landour, North West Provinces, India. He was educated at Stokes's School, Mussoorie, India, and at the Universities of Marburg and Edinburgh, where he graduated M.B., Ch.B. in 1901. After holding the post of resident surgeon at the Royal Maternity Hospital, Edinburgh, he entered the Indian Medical Service in 1902 and worked for the next three years with the Aden Boundary Commission on a study of malarial parasites. Thereafter he undertook special duties at the King Institute of Preventive Medicine in Madras, when he began an investigation into the aetiology of kala-azar. From 1907 to 1914 he was assistant director at the King Institute, and he spent some time studying the causes of Oriental sore. During the first world war he served as entomologist with the Mesopotamian Expeditionary Force and was mentioned in dispatches.

After the war he worked as director of the Pasteur Institute, Southern India, until 1921, when he came back to Britain and was appointed lecturer in medical entomology and parasitology at the University of Edinburgh, being elected a Fellow of the Royal Physical Society of Edinburgh. In 1925 he went to North China in charge of the Royal Society's Kala-azar Commission. On his return he was appointed professor of entomology at the University of Liverpool and held this chair until ill-health forced him to retire in 1937. On his retirement he was appointed emeritus professor and was awarded the Mary Kingsley medal by the Liverpool School of Tropical Medicine.

Professor Patton was the author of numerous papers and books, perhaps the best known being *Insects, Ticks, Mites and Venomous Animals of Medical and Veterinary Importance*. This formidable textbook was to have been in three volumes, but only two were completed owing to his premature retirement. His *Textbook of Medical Entomology*, which he wrote jointly with F. W. Cragg and which was published in 1913, also achieved fame.

On his retirement he made his home in Torrington, Devon. He is survived by his widow and five sons.

R. M. G. writes: The Indian Medical Service includes in its rolls many distinguished research workers, and among them the name of Walter Scott Patton ranks high. During his earlier years in the Service, when the greater part of his time was occupied by routine duties, his research work could be carried on only in the short leisure hours which most men devote to recreation. Yet he contrived to publish many papers during that period, and when later he was relieved of much of the routine he rapidly achieved a world-wide reputation as an authority on medical entomology. Among his many contributions to this branch of science the most important are his studies on the myiasis-producing flies, insects which he knew to cause great suffering among the indigent population in India.

Nor was he only a research worker. He was a teacher in the best and widest sense of the word, one who studied and taught all that was most valuable in the work of others, and enriched it with his own contributions to knowledge and learning. To-day, all over the world, there are hundreds of students who remember Patton as an outstanding teacher, and many thousands who have been helped and guided by his books and other contributions to scientific literature.

The whole of Patton's long life was unremittingly and unostentatiously devoted to the service of humanity, a devotion which was deeply rooted in his religious convictions and always directed to the relief of suffering. We who had the privilege of being his colleagues realize how deeply and sincerely this shy and sensitive man sought to help everyone with whom he came into contact, particularly those who were in any way sad or distressed, and we know how students of all nationalities benefited from his influence, not only in the university classrooms but also in his home, where he and his charming and devoted wife extended hospitality to students of every race and creed.

IDA S. SCUDDER, M.D., D.Sc., F.A.C.S.

Dr. Ida S. Scudder, founder of the Christian Medical College at Vellore, died at Kodaikanal, South India, on May 24. She was 90 years of age.

We are indebted to Dr. R. G. COCHRANE for the following tribute: Dr. Ida Scudder came from a missionary family which has given one thousand years to missionary service.

She was rightly revered and venerated in India as one of the most saintly of women. The story of her accomplishments is a saga of missionary history.

When Ida Scudder was a young girl visiting her parents in India in the year 1890 she was so challenged with the crying need to help the women of that country that she returned to America and entered the Women's Medical College in Philadelphia in 1895, at a time when it took courage for a woman to study medicine. In 1898 she transferred to Cornell Medical College when women were first admitted on an equality with men. Ida S. Scudder, with a sense of Divine calling, went back to India (where her father and her grandfather had worked) and started a small hospital in Vellore, in South India. From this small beginning, through Dr. Ida's courage and faith, and her determination to bring to India's women the benefits of modern medicine and surgery in a Christian background, arose what is now one of the finest medical colleges in the East—the Christian Medical College, Vellore.

Dr. Ida Scudder's name attracted men and women of outstanding ability on to the staff. One only needs to mention the work of Mr. Paul Brand, who has made such fine contributions to the relief of deformity in leprosy. It was through Dr. Scudder's vision, through her skill as a surgeon, through her competence as an administrator, that the impossible became possible, for without her exceptional talents the way could never have been prepared for the development of a women's medical school of lower grade into the first-class medical college that now stands in Vellore. The name of Ida S. Scudder will go down in missionary history along with those of such pioneers as Livingstone of Africa, Christie and Thomas Cochrane of China, Wanliss and Edith Brown of India, and Schweitzer of Lamberene, the doyen of medical missionaries to-day.

As one who is privileged to have been associated with Dr. Ida S. Scudder, and who followed her as principal of the Christian Medical College, Vellore, my outstanding impression is her faith in God, her loyalty, her devotion, and her determination to give of her best to the India she loved; hers was a Christian dedication which was an inspiration and a challenge to men and women of all faiths.

Dr. Scudder died at the ripe age of 90. Her influence will continue so long as India remains. The aura of her greatness will be felt in the corridors of the institution which she created. Her high ideals of service will still inspire all those who pass through the portals of the College to high endeavour. The vision and imagination of this outstanding medical woman, whose life transcended all barriers of race and nationality, is an example to the whole world of the meaning of practical Christianity. The College which she founded will stand as a memorial and as a reminder of a faith which knew no obstacles, an imagination which envisioned the impossible, of a life utterly committed to God, for, truly, she was a Christian both in deed as well as in word.

Medico-Legal

A.I.D. AND NULLITY

[FROM OUR LEGAL CORRESPONDENT]

A decision of considerable importance to medical practitioners advising the use of A.I.D. was made by Mr. Commissioner Latey, Q.C., in the Divorce Court on May 11 (*The Times*, May 12).

One of the grounds upon which a decree of nullity of marriage will be pronounced is the impotence of the respondent spouse. Impotence is defined as inability to consummate the marriage by ordinary intercourse. To be a ground for a decree, the impotence must have existed at the time of the marriage and continue to exist at the date of the hearing. It is a good defence to a petition for nullity on this ground that the petitioner has approbated the marriage. If a spouse takes advantage of the benefits of a marriage, waiving certain rights under it, the courts will not then assist that spouse to claim that the marriage be declared void on the strength of the very rights waived. However, one cannot be said to waive one's rights unless one knows what those rights are. The petitioner's knowledge of the remedies available is therefore clearly vital to the question of approbation.

Question of Approbation

In the present case, the parties went through a ceremony of marriage in 1944. At the time of the ceremony the husband was impotent as a result of accidental electric burning: there was no possibility of any improvement. The wife now petitioned for a decree of nullity, and the suit was not defended; but the court was constrained to take notice of the possible bar to a decree arising out of the fact that the wife had, with the consent of her husband, resorted to A.I.D. and as a result had given birth to a child in June, 1950. The question arose whether on these facts the wife had approbated the marriage.

Few doubt that the question of approbation depends on the intention and knowledge of the spouse in doing the acts in question. It is no approbation of a marriage to have had a child by A.I.D. if the petitioner showed a desire for a normal marriage and did not acquiesce in the situation, or if the petitioner was unaware at the time of the facts or of the law giving rise to a remedy in the form of a decree of nullity. Mr. Commissioner Latey held that on the evidence in the present case it was clear that the wife, at the time she resorted to A.I.D., had no knowledge of the legal remedy open to her in respect of her husband's incapacity. The resort to A.I.D. therefore did not amount to approbation, and the wife was entitled to a decree.

In the course of his judgment, Mr. Commissioner Latey referred to the Report of the Royal Commission on Marriage and Divorce, 1956. In their Report, after summarizing the law on nullity, the Commission recommended that, where the parties had gone to the length of artificial insemination of the wife, that constituted such a fundamental step that it was undesirable that they should thereafter be permitted to claim that the marriage was void on the ground of the impotence of either of them. This recommendation has not, however, been acted upon by the legislature. In 1959, in a memorandum* to the Departmental Committee on Artificial Insemination, the council of the Law Society recommended that, where a child is born as a result of A.I.D. to which the husband has consented, nullity proceedings by either spouse on the grounds of inability or wilful refusal to consummate should be excluded by statute, but not where insemination is unsuccessful.

Danger of Later Bastardization

The central problem arising out of the present state of the law is the status of the child born as a result of A.I.D. The child of a woman who is lawfully married but upon whom he is begotten by someone other than her lawful husband is illegitimate, save that there is a presumption of legitimacy the effect of which is that the child is presumed to be legitimate until proved otherwise beyond reasonable doubt. Proof of impotence would involve rebuttal of this presumption and hence bastardize the child. Practitioners recommending, or being asked for, A.I.D. in cases where one of the spouses is impotent should therefore bear in mind the possible results for the child if the marriage is eventually nullified. Such practitioners may well feel themselves under a duty not to assist in the conception of a child which may be thus bastardized—that is, they may feel that they ought not to assist in A.I.D. where one of the spouses does not acquiesce in a voidable marriage, and in all cases ought to ensure that the injured spouse knows of the possibility of a nullity decree before embarking on A.I.D.

*See *British Medical Journal*, 1959, **2**, 584.

Universities and Colleges

UNIVERSITY OF OXFORD

In Congregation on June 2 Sir Howard Florey, M.D., F.R.C.P., F.R.S., was elected a member of the Visitatorial Board from the first day of Michaelmas Term, 1960, until the first day of Hilary Term, 1962.

In Congregation on June 4 the following degrees were conferred:

D.M.—C. J. Dickinson, H. C. Nohl.
B.M.—R. Cook.

UNIVERSITY OF CAMBRIDGE

Dr. Moises Derechin has been elected to a Broodbank Fellowship for two years from October 1, 1960.

UNIVERSITY OF LONDON

On March 30 the degree of M.D. was awarded by the Senate to P. T. Flute (*corrected announcement*).

Dr. A. J. Buller, Senior Lecturer in Physiology at St. Thomas's Hospital Medical School, has been appointed to the University Readership in Physiology tenable at King's College.

Mr. D. F. N. Harrison, Senior Registrar to the Ear, Nose, and Throat Department at Guy's Hospital, has been appointed to the University Readership in Laryngology tenable at the Institute of Laryngology.

UNIVERSITY OF BIRMINGHAM

The title of Professor of Immunological Pathology has been conferred on Dr. P. G. H. Gell, Reader in Experimental Pathology, from October 1, 1960.

Dr. D. R. MacMillan has been appointed Research Fellow in the Department of Paediatrics and Child Health.

The Leonard Parsons Memorial Lectures in 1961 will be delivered by Professor Lawson Wilkins, Associate Professor of Paediatrics in Johns Hopkins University, Baltimore, U.S.A.

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

At a meeting of the College held on June 3, with the President, Dr. P. T. O'Farrell, in the chair, the following members were admitted to the Fellowship: J. D. Whiteside, Patricia M. Alston, Joan M. Mullaney.

The President then admitted M. B. Levine to the Membership, and J. Alvey, P. Donnelly, J. B. Hourihane, and C. F. McCarthy to the Licence and Membership of the College.

ROYAL COLLEGE OF SURGEONS IN IRELAND

The Fellowship of the College was conferred upon R. L. Agarwal on June 1.

FACULTY OF ANAESTHETISTS

The President, Vice-President, and Council of the Royal College of Surgeons in Ireland have awarded the Fellowship of the Faculty of Anaesthetists of the College to the following: Dr. T. J. Gilmartin, Dean; Dr. V. O. McCormick, Vice-dean; and Drs. P. Drury Byrne, P. Nagle, S. Kenny, P. Murray, J. Woodcock, R. Davys, J. Dundee, S. Love, K. Bayne, W. Bingham, S. Bose, J. Boyd, J. D. Bourke, G. J. C. Brittain, A. B. Bull, F. M. Byrn, D. G. Coleman, W. S. Davis, J. B. Glynn, T. F. Heavey, J. C. Hewitt, A. H. Kasasian, O. V. S. Kok, M. V. Lemon, B. Lyne, P. R. Mersham, M. Murphy, J. MacAuley, M. O'Connor, and S. D. Oliver, Lady Read, Drs. D. L. Scott, R. W. Shaw, M. A. Woods, and Z. Lett.

Other Fellows will be elected at a later date and a list of names will be published in due course. Anaesthetists of distinction may still make application for the award.

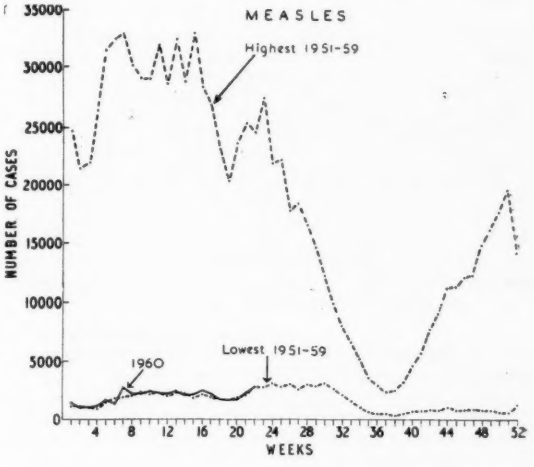
Vital Statistics

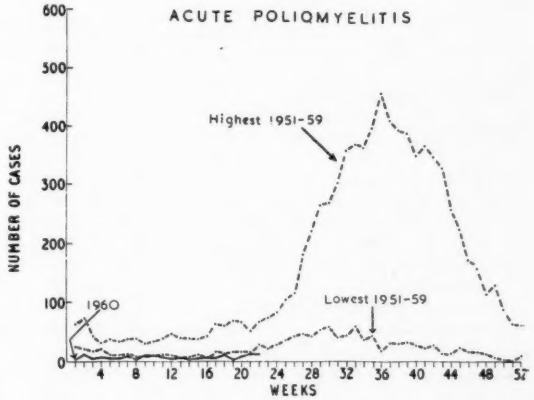
Road Deaths in April

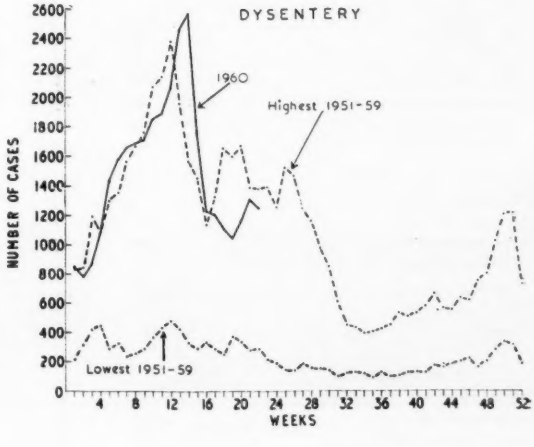
Five hundred people were killed as a result of road accidents in Great Britain during April—44 more than in April last year, and 90 more than in 1958. The total number of killed and injured was 26,948—nearly 11% more than in April, 1959. The volume of motor traffic, however, was 15% higher in 1960. Motor-cyclists and their passengers suffered the greatest numerical increase in casualties, but there were 433 fewer casualties among pedal cyclists.

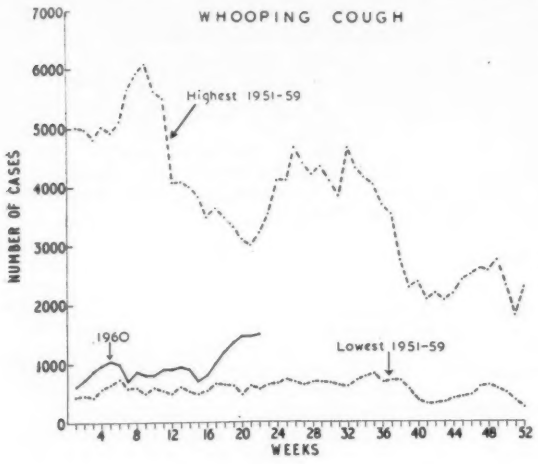
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1951–9 are shown thus - - - - - -, the figures for 1960 thus ———. Except for the curves showing notifications in 1960, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available.

	Week Ending May 28	Week Ending June 4
Measles		
Lancashire	794	**911**
Liverpool C.B.	188	**291**
Manchester C.B.	96	**115**
Dysentery		
Cheshire	26	**47**
Birkenhead C.B.	7	**15**
Wallasey C.B.	10	**20**
Devonshire	10	**29**
Plymouth C.B.	6	**22**
Durham	39	**34**
Seaham U.D.	11	**23**
Lancashire	239	**223**
Bolton C.B.	9	**13**
Liverpool C.B.	23	**19**
Manchester C.B.	10	**16**
Accrington M.B.	16	**19**
Failsworth U.D.	6	**11**
Morecambe and Heysham M.B.	27	**23**
Urmston U.D.	10	**13**
London	173	**202**
Bermondsey	6	**11**
Islington	52	**61**
Lambeth	6	**15**
Lewisham	5	**13**
St. Pancras	10	**16**
Southwark	5	**11**
Wandsworth	23	**24**
Nottinghamshire	60	**63**
Carlton U.D.	10	**10**
Worksop R.D.	36	**36**
Yorkshire West Riding	165	**145**
Barnsley C.B.	22	**12**
Bradford C.B.	26	**25**
Dewsbury C.B.	5	**15**
Huddersfield C.B.	16	**15**
Leeds C.B.	19	**24**
Sheffield C.B.	45	**19**
Glasgow	113	**106**
Food-poisoning		
Lancashire	38	**46**
Liverpool C.B.	10	**15**
Accrington M.B.	2	**14**

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **May 28** (No. 21) and corresponding week 1959.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1960 Eng. & Wales	1960 Lond.	1960 Scot.	1960 N. Ire.	1960 Eire	1959 Eng. & Wales	1959 Lond.	1959 Scot.	1959 N. Ire.	1959 Eire
Diphtheria	2	1	1	0	1	3	0	0	0	1
Dysentery	1,312	173	191	20	3	943	83	268	8	5
Encephalitis, acute	4	0	1	0		3	0		0	
Enteric fever:										
Typhoid	3	2	0	0		0	0	0	1	1
Paratyphoid	3	1	0	0		7	1	4(B)	0	2(B)
Food-poisoning	157	9	43	3		280	51	14	0	
Infective enteritis or diarrhoea under 2 years				22	27				6	19
Measles*	2,254	99	33	7	34	16,932	687	473	404	142
Meningococcal infection	25	3	8	0	2	24	2	15	1	2
Ophthalmia neonatorum	21	0	5	0		37	5	3	0	
Pneumonia†	256	17	185	7	5	232	9	142	4	2
Poliomyelitis, acute:										
Paralytic	6	2	0	} 0	2	{ 23	7	1	} 0	
Non-paralytic	6	2	0			{ 6	3	1		
Puerperal fever§	196	19	18	0		208	39	10	0	1
Scarlet fever	606	35	56	9	12	675	36	66	24	21
Tuberculosis:										
Respiratory	459	66	76	23		551	54	88	19	
Non-respiratory	69	3	14	5		72	6	17	2	
Whooping-cough	1,453	124	223	5	90	627	15	65	20	55

DEATHS	1960 Eng. & Wales	1960 Lond.	1960 Scot.	1960 N. Ire.	1960 Eire	1959 Eng. & Wales	1959 Lond.	1959 Scot.	1959 N. Ire.	1959 Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery	1	0		0		0	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	8	0	5	0	0	6	0	2	0	1
Influenza	10	0	1	0	1	9	0	0	0	0
Measles		0	0	0	0		0	0	0	0
Meningococcal infection		0	0				0	1		
Pneumonia	480	41	15	9	3	427	25	21	16	7
Poliomyelitis, acute	0	0		0	0	5	1		0	0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	} 68	{ 1	6	0	4	} 68	{ 3	3	0	1
Non-respiratory		1	0	0	2		2	2	0	0
Whooping-cough	1	0	0	0	0	0	0	0	0	0
Deaths 0–1 year	349	35	30	6	10	299	32	31	7	12
Deaths (excluding stillbirths)	9,305	713	577	114	132	8,770	655	590	120	162
LIVE BIRTHS	15,793	1390	1055	308	380	16,380	1368	974	291	458
STILLBIRTHS	333	25	18			345	30	22		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Patrick Buxton Memorial Prize

A Patrick Buxton Memorial Prize has been endowed by the relatives of the late PATRICK BUXTON, F.R.S., who was director of the department of entomology at the London School of Hygiene and Tropical Medicine from 1926 and professor from 1933 until his death in 1955.

The prize of £150, to be awarded for the first time in 1961, will be for the best essay relating to medical or veterinary entomology or an allied subject based on the candidate's published or unpublished research. Candidates must be past or present students of the School or members of the School staff. Essays should reach the Dean, London School of Hygiene and Tropical Medicine, Keppel Street (Gower Street), London, W.C.1, by March 31, 1961.

Unsaturated Fats and American F.D.A.

The American Food and Drug Administration has declared in its *Federal Register* that any claim, direct or implied, in the labelling of fats and oils or other fatty substances offered to the general public that they will prevent, mitigate, or cure diseases of the heart or arteries is false or misleading, and constitutes misbranding within the meaning of the Federal Food, Drug, and Cosmetic Act.

The Administration gives as its reasons that the role of cholesterol in heart and artery diseases has not been established; that a causal relationship between blood cholesterol levels and those diseases has not been proved; and that it has not been demonstrated that it is advisable for Americans to make extensive changes in the nature of the fat they eat.

"Imferon" Withdrawn in U.S.A.

At the request of the Food and Drug Administration of the U.S.A., Lakeside Laboratories Inc. have withdrawn the iron-dextran complex, imferon, from the market there. A letter to all American physicians from the firm's executive vice-president states: "We are, of course, electing to withdraw the drug from the market without a hearing rather than risk aggravating the current cancer scare in this country. Because imferon is such an unusually useful drug, we are in the process of setting up a totally independent and impartial medical committee to screen the available facts and suggest a future course of action."

Victoria Hospital, Kirkcaldy

A substantial extension to the Victoria Hospital, Kirkcaldy, has recently been completed at a cost of £750,000. It is the first phase of a scheme designed to provide improved hospital facilities for East Fife.

The main building is a three-story block housing 123 patients, a twin operating suite, physiotherapy department, radiography department, a pharmacy and central sterilizing department, out-patients' departments for chest, eye, paediatric, dermatology, and psychiatric clinics, as well as the usual offices and a medical residency. A single-story wing at right angles to the main block contains the main out-patients' department. An audio-frequency call system enables doctors to be quickly traced through the receiver each carries in his pocket. The new operating theatre suite is supplied with dust-free air, automatically heated and humidified, and electronically controlled by the theatre staff. The theatres are heated by steel pipes embedded in special plaster ceilings which warm the rooms by radiation to avoid creating convection currents which might raise dust particles from the floor. A self-contained minor theatre communicates directly with the radiography department by means of an electrically controlled cassette hoist. In addition to the main building there is a six-story nurses' home, a new kitchen and dining-hall, and boiler house and mortuary blocks.

Chair of Pathology, Durham University

Dr. A. G. HEPPLESTON, senior lecturer in pathology at the Welsh National School of Medicine, has been appointed to the chair of pathology at Durham University, tenable in the Newcastle Division.

Dr. Heppleston, who is 44, was educated at Manchester Grammar School and the Victoria University of Manchester. He graduated M.B. with honours in 1938, became M.R.C.P. (London) in 1941, and took his M.D. with commendation in 1954. He was medical chief assistant at Manchester Royal Infirmary before becoming assistant lecturer in pathology in the Welsh National School of Medicine. After holding a Dorothy Temple Cross Research Fellowship in the University of Pennsylvania, he returned to the University of Wales to take up his present post in 1948. His published work has largely concerned pulmonary pathology, both human and experimental, especially in relation to the pneumoconioses, fibrocystic states of the lung, the various forms of emphysema, the pathogenesis of airborne tuberculosis, and serum polysaccharide changes in different disease processes.

Association of Police Surgeons

At the annual conference of the Association of Police Surgeons of Great Britain, held at Cheltenham from May 25 to 28, Dr. R. HUNT COOKE was elected President. The proceedings included a demonstration of the "breathalyser" by Dr. R. D. SUMMERS, the retiring President, and a brains trust in which the panel included Dr. F. E. CAMPS and the Chief Constable for Gloucestershire.

Charterhouse Rheumatism Clinic

Lord COHEN OF BIRKENHEAD gave the Gilbert Scott memorial lecture in London on June 10, his subject being "The Present Status of Collagen Diseases." The lecture commemorates Dr. S. Gilbert Scott, much of whose work on the treatment of rheumatism with *x* rays was done at the Charterhouse Clinic.

After the lecture the governors and medical staff of the Clinic gave a dinner to Lord Cohen at the Royal Society of Medicine. The DUCHESS OF GLOUCESTER was present as president of the Clinic, and her health was proposed by Mr. LLEWELLYN B. DART, chairman of its governing body. Lord COHEN OF BIRKENHEAD replied to the toast to his health proposed by Sir HENEAGE OGILVIE.

Lady Tata Memorial Trust

The Trustees of the Lady Tata Memorial Trust have renewed or made the following awards for research on leukaemia and allied diseases in the Academic Year beginning October 1:

Grants for research expenses, Dr. B. M. Braganca (Indian Cancer Research Centre, Bombay); Dr. J. Pontén (Pathology Institute, Uppsala); Dr. M. Simonsen (Institute of Pathological Anatomy, Copenhagen); Dr. H. J. Woodliff* (New Pathological Laboratory, Radcliffe Infirmary, Oxford). *Scholarships*, Dr. L. Chieco-Bianchi* (Institute of Pathological Anatomy, Bari); Dr. J. Hastrup (Institute of General Pathology, Aarhus).

*New award.

Part of the new main building, Victoria Hospital, Kirkcaldy. [*Alastair Hunter, Edinburgh*

In Brief

A B.E.A. air ambulance is to be named "Sister Jane Kennedy" as a tribute to the nursing sister, who, with the crew of two, died when an air ambulance Heron crashed on Islay in the Inner Hebrides three years ago.

People in the News

Sir SELWYN SELWYN-CLARKE has been invited by the South Pacific Commission to attend the annual meeting of its Research Council in July to advise on health matters. Details of the Commission's work were given in the *Journal* of May 21 at the foot of p. 1541.

COMING EVENTS

Cambridge Graduates' Medical Club.—Annual general meeting and dinner, Pembroke College, July 1. Members who have not received notification or other Cambridge men interested please write immediately to Mr. H. E. BATTEN, 67, Bridge Street, Cambridge.

Postgraduate Medical School and Hammersmith Hospital Association.—Open day, July 8, 10 a.m., including ward rounds, films, and clinicopathological conference on "Vascular Complications of Mitral Stenosis" and "Islet Cell Tumour of the Pancreas."

British Council for Rehabilitation.—Course and conference, "Rehabilitation—From Incapacity to Capacity," Dublin, July 12–14. Details from General Secretary, British Council for Rehabilitation, Tavistock House South, Tavistock Square, London, W.C.1. (Euston 4037–8.)

Schorstein Memorial Lecture: London Hospital Medical College.—Sir MACFARLANE BURNET, O.M., F.R.S., "Tissue Transplantations: Potentialities and Limitations," July 13, 5.15 p.m., the College Hall, Ashfield Street, London, E.1. Admission by ticket from the Secretary, The London Hospital Medical College, Turner Street, London, E.1.

Society of Medical Officers of Health: College of General Practitioners.—Joint Conference, July 16–17, Medical School, Birmingham University. Details from Dr. J. BEATSON HIRD, 97, Hillmeads Road, King's Norton, Birmingham, 30.

Central Council for Health Education.—Summer School: "Health Education," August 9–19, Froebel Educational Institute, Grove House, Roehampton Lane, London, S.W.15. Details from the Council, Tavistock House North, Tavistock Square, W.C.1.

British Association for Advancement of Science.—Annual meeting, Cardiff, August 31–September 7. Evening discourses include Professor E. B. CHAIN, F.R.S., on "Microbiological Methods in the Development of Drugs."

4th International Criminological Congress.—The Hague, September 5–12. Details from the secretariat of the Congress, 14, Burgemeester de Monchyplein, The Hague, Netherlands.

1st European Congress of Child Psychiatry.—"Maturation: its Biological Basis, Stages, and Social Implications," also symposium on "Child Psycho-analysis," New School of Medicine, 45, Rue des Saints Pères, Paris, 6, September 16–20. Details from Dr. D. J. DUCHÉ, Pavillon Clérambault, Hôpital de la Salpétrière, 47, Boulevard de l'Hôpital, Paris, 13, France.

3rd European Congress of Cardiology.—Rome, September 18–24, 1960. Details from Dr. V. PUDDU, Clinica Medica, Policlinico Umberto 1, Rome.

Czechoslovak Congress of Rheumatology.—Pieštany, Czechoslovakia, September 21–25. Details from the Secretariat of the Congress, 4, Na Slupi, Prague, 2, Czechoslovakia.

1st International Congress on Medical Photography.—Düsseldorf, September 27–30, 1960. Details from Deutsche Gesellschaft für Photographie eV, 49, Neumarkt, Cologne, Germany.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, June 20

LONDON UNIVERSITY.—At University College Hospital Medical School, 5 p.m., special university lecture in medicine by Professor N. C. Louros (Athens): Reduction of Pain During Labour and Delivery.
MARLBOROUGH DAY HOSPITAL.—8.15 p.m., Professor Leonhard (Berlin): Treatment of Ideohypochondriac and Sensohypochondriac Neuroses.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. Brian Ackner: Anorexia Nervosa.

Tuesday, June 21

INSTITUTE OF DERMATOLOGY.—At British Institute of Radiology, 5 p.m., Dr. P. Wade: Radiotherapy of Malignant Skin Conditions, II.
LONDON UNIVERSITY.—At London Hospital Medical College, Turner Street, E., 5 p.m., Dr. Austin T. Moore (Moore Clinic, Columbia, South Carolina): Surgery of the Hip, with Special Reference to Moore Arthroplasty.
ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., Mitchell Lecture by Dr. J. G. Scadding: Mycobacterium Tuberculosis in the Aetiology of Sarcoidosis.
SOUTH-WEST LONDON MEDICAL SOCIETY.—At Bolingbroke Hospital, 8.30 p.m., Mr. R. G. Thomas: Surgery of the Hip-joint.

Wednesday, June 22

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. W. Riddell: Infections due to Yeasts.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. S. W. A. Kuper: B.C.G. Vaccination and Leprosy.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Professor S. D. Elek: Cytomegalic Inclusion Body Disease.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Arnott Demonstration by Miss J. Dobson: A Hitherto Undescribed Section of John Hunter's Museum.

Thursday, June 23

INSTITUTE OF CHILD HEALTH.—5 p.m., Dr. Edith L. Potter (Chicago): Perinatal Mortality Studies at the Chicago Lying-in Hospital.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. Brian Russell: Uncommon Skin Tumours, Clinical and Pathological.
LONDON JEWISH HOSPITAL MEDICAL SOCIETY.—At Medical Society of London, 8.15 p.m., annual general meeting.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. R. J. G. Sinclair: The Marfan Syndrome.
●ROYAL COLLEGE OF NURSING FOUNDERS' LECTURE.—At Porchester Hall, Porchester Road, London, W.2, 8 p.m., Lord Cohen of Birkenhead: The Control of Disease.

Friday, June 24

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. Brian Russell: clinical demonstration.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. F. J. Prime: clinical demonstration.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—10 a.m., Mr. G. W. Taylor: Primary Lymphoedema.

APPOINTMENTS

BIRMINGHAM REGIONAL HOSPITAL BOARD.—F. J. Davis, F.F.A. R.C.S., M.R.C.S., L.R.C.P., Part-time Consultant Ananaesthetist to Shrewsbury Group and Robert Jones and Agnes Hunt Orthopaedic Hospital; H. G. Lowe, M.B., Ch.B., F.R.C.S., Part-time Consultant Orthopaedic Surgeon to Stafford Group; J. D. Bourke, M.B., B.Ch., F.F.A. R.C.S., Part-time Consultant Anaesthetist, and M. J. D. Noble, M.B., Ch.B., F.R.C.S.Ed., M.R.C.O.G., Part-time Consultant Obstetrician and Gynaecologist, both to Birmingham (Dudley Road) Group; R. A. Chand, M.B., Ch.B., Whole-time Assistant Chest Physician to Wolverhampton and Dudley and Stourbridge groups of hospitals and Wolverhampton County Borough Council; E. F. Bowers, M.B., B.S., D.C.P., D.Path., Whole-time Consultant Pathologist to Dudley and Stourbridge group of hospitals.

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—C. R. Jolly, M.B., B.S., F.F.A. R.C.S., D.A., Consultant Anaesthetist, Ipswich and East Suffolk Hospital Group; B. S. Phillips, M.B., B.Chir., Senior Registrar to Department of Child and Family Psychiatry, Ipswich and East Suffolk Hospital; J. P. Duffy, M.B., Ch.B., Medical Registrar, West Suffolk General Hospital.

HOSPITAL FOR SICK CHILDREN, Great Ormond Street, London, W.C.—J. N. Mishra, M.B., B.S., M.R.C.P.Ed., D.C.H., Medical Registrar; J. C. Pisarello, M.D., Resident Medical Officer to Department of Neurology and Neurosurgery; O. Ransome-Kuti, M.B., B.Ch., Assistant Resident Medical Officer, Tadworth Court; A. G. C. Renwick, M.B., Ch.B., Registrar to Department of Chemical Pathology; G. R. Parry, M.B., B.S., F.R.C.S., Surgical Out-patient Assistant; C. E. Forbes, M.D., C.M., and S. R. McKay, M.B., B.S., D.T.M.&H., House-physicians.

MANCHESTER REGIONAL HOSPITAL BOARD.—P. R. Stevens, M.R.C.S., L.R.C.P., D.O., Consultant Ophthalmologist (eight half-days weekly) to Blackburn and District Group of Hospitals; V. H. Wheble, B.M., B.Ch., F.R.C.S.Ed., Consultant Traumatic and Orthopaedic Surgeon to Ashton, Hyde and Glossop Group of Hospitals.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Wilkie.—On June 9, 1960, at Simpson Memorial Maternity Pavilion, Edinburgh, to Jean Catherine, wife of Lindsay Wilkie, M.St.J., L.R.C.P. and S.Ed., L.R.F.P.S., a brother for Joyce, Sandra and Yvonne—James Ritchie.

DEATHS

Cowan.—On May 26, 1960, at Edinburgh, Alexander Rea Cowan, M.B., Ch.B., D.M.R., late of 28, Blackford Avenue, Edinburgh.
Gerrard.—On May 26, 1960, Alfred Henry Gerrard, M.D., M.R.C.P., D.P.H., of Little Hintock, Deepdene Park Road, Dorking, Surrey, formerly of Wimbledon, London, S.W., aged 91.
Simpson.—On May 25, 1960, at Dulwich, London, S.E., James Simpson, M.B., Ch.B., of 7, Courtrai Road, Forest Hill, London, S.E.

Any Questions ?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Investigation of Patients who Bleed

Q.—*What are the minimal laboratory investigations necessary to exclude blood dyscrasia in patients who give a history of prolonged bleeding?*

A.—It should be stressed that at present there is no single group of laboratory tests which will give a definite answer in every patient suspected of having a bleeding disorder. In the mild cases with equivocal laboratory results the patient's personal history and family history are of great importance. If there is a definite history of excessive bleeding after dental extraction and tonsillectomy, then, even if the tests of clotting function are normal, the patient should be considered to be a "bleeder." The diagnosis is further strengthened if other members of the family have had similar trouble.

The following laboratory tests should, in the majority of cases, be able to confirm or exclude the presence of a blood disorder which would be likely to endanger the patient's life. The tests should include: examination of a stained blood film; white cell count; platelet count; bleeding time; tourniquet test; whole-blood clotting time (Lee and White method); 1 stage prothrombin time; and thromboplastin generation test.

Examination of a blood film along with a platelet count and a white cell count is an essential first step to exclude thrombocytopenia or leukaemia, or some related condition, as the cause of the increased bleeding. The tourniquet test and the bleeding time, when considered along with the other tests, can give useful information in platelet and vascular abnormalities. Even in the absence of any other abnormality, the finding of a definite prolongation of the bleeding time should make one cautious of undertaking surgery, since many of these patients bleed excessively during or after operation. The whole-blood clotting time, despite its limitations, is a useful screening test for the severer forms of haemophilia, since in this country a marked prolongation of the clotting time (15 minutes or more) in a male signifies haemophilia in 9 out of 10 cases. The thromboplastin generation test is at present the most sensitive method of demonstrating inability to form thromboplastin normally and as such is invaluable in the diagnosis of Christmas disease and haemophilia. In the mild forms of these two conditions this test may be almost normal, in which case the level of the factors must be assayed in order to settle the question.

REFERENCE

[1] Biggs, R., and Macfarlane, R. G., *Human Blood Coagulation and its Disorders*, 1957. Blackwell Scientific Publications, Oxford.

Vitamin-E Therapy

Q.—*What, if any, are the indications for vitamin-E therapy?*

A.—So far as man is concerned it has never been conclusively proved that there is a specific disease which is due to deficiency of vitamin E and which can be cured by administration of the vitamin. In most animals, however, lack of vitamin E in the diet does lead to illness. The clinical features of this illness vary in different species, but the two most prominent manifestations are a failure of normal reproduction and muscular dystrophy. In clinical medicine, therefore, vitamin E has been advocated mainly for the treatment of such conditions as recurrent abortion, toxaemia of pregnancy, muscular dystrophy, and motor neurone disease. Although several workers have claimed that it is effective in these conditions the results have not been confirmed in critical studies, and it has not been proved conclusively that vitamin E is any better than a placebo. Some of those who advocate its use believe that good results are obtained only when the naturally occurring vitamin is used in the form of wheat germ, and that synthetic alpha-tocopherol, which is the substance most often prescribed, is not so effective. In recent years vitamin E has been recommended for the treatment of intermittent claudication. Conflicting results have been reported, and at the moment the fairest appraisal of the value of this form of therapy in a condition of such spontaneous variability as intermittent claudication is the Scottish verdict of "not proven." There is no evidence to support the claim that vitamin E is of value in other forms of cardiovascular disease, such as coronary atherosclerosis. There have also been reports that vitamin E is of value in Dupuytren's contracture, but few surgeons are impressed with the results. In short, although much therapeutic zeal has been expended in trying to find a clinical use for vitamin E and a voluminous literature exists, there are at present no clear-cut indications for its therapeutic use in man.

Chlorpromazine and Morphine

Q.—*May chlorpromazine be mixed in the same syringe with morphine to prevent vomiting?*

A.—Morphine and chlorpromazine are not chemically incompatible, and from this point of view there is no reason why the two drugs should not be mixed in the same syringe and given together. The choice of chlorpromazine as the anti-emetic agent for this purpose may be questioned. Both chlorpromazine and morphine are central nervous depressants, and chlorpromazine potentiates the action of most analgesics and sedatives. Moreover, both drugs are apt to produce marked postural hypotension in some subjects. If the intention is merely to prevent the nausea and vomiting caused by the opiate and not to increase the amount of sedation, then, if chlorpromazine is used, a dose of 25 mg. should be sufficient. According to Moyer[1] diphenhydramine, dimenhydrinate, cyclizine, and meclozine are more effective than chlorpromazine in combating the nausea and vomiting induced by opiates. Since these anti-emetic substances are all less apt to cause side-effects than chlorpromazine, one of them would be more appropriate. They are all quite rapidly absorbed when taken orally, and therefore they should be given by this route rather than parenterally, unless the patient is already vomiting.

REFERENCE

[1] Moyer, J. H., in *Drugs of Choice, 1958-59*, 1958, edited by W. Modell. Henry Kimpton, London.

Liquoid in Blood Cultures

Q.—*What is the value of "liquoid" (sodium polyanethol sulphonate) when added to blood cultures?*

A.—The blood in some bacteriaemic infections, notably subacute bacterial endocarditis, is self-sterilizing *in vitro*, and liquid cultures made in the ordinary way may therefore yield no growth unless the blood is much diluted in the medium (this difficulty applies less to pour plates made with the patient's blood, in which colonies often appear before any growth occurs in broth and sometimes when broth cultures remain sterile). Liquoid is both an anticoagulant and an agent destroying the bactericidal power of the blood: it exerts this effect by neutralizing both complement and antibodies. The concentration in which it should be present in the final mixture of blood and medium is 0.05%: it may be either used initially as the anticoagulant or incorporated in the medium. It withstands autoclaving and is stable during storage. Its use for this purpose is largely based on the work of T. von Haebler and A. A. Miles,[1] who, among other observations, inoculated fresh sterile difibrinated blood, with or without liquoid, with small numbers of various bacteria: many species were destroyed in the absence of liquoid, but all grew freely when it was present.

REFERENCE

[1] von Haebler, T., and Miles, A. A., *J. Path. Bact.*, 1938, **46**, 245.

Swelling of Extremities After Alcohol

Q.—*What could be the cause of swelling of the feet and fingers in an otherwise fit young woman about 10 minutes after taking even a small amount of alcohol? Her feet tend to swell in very hot weather, but not from other causes.*

A.—It is likely that the cause in an otherwise fit patient is a simple allergy, possibly related to local vasodilatation. There are, however, a number of pathological conditions in which undue sensitivity to alcohol is recognized. Patients with malignant lymphomata, particularly of the Hodgkin's variety, sometimes complain of considerable pain after consumption of alcohol.[1] Hypersensitivity has also been noted in carcinoid tumours,[2] and other features such as flushing, gastrointestinal, and cardio-respiratory symptoms would support this diagnosis. Finally, sensitivity to alcohol as well as to drugs such as barbiturates can occur in porphyria. The last two conditions may be excluded by biochemical examination of the urine for metabolic products of serotonin and for porphobilinogen respectively.

REFERENCES
1 *Brit. med. J.*, 1956, **2**, 652.
2 Snow, P. J. D., Lennard-Jones, J. E., Curzon, G., and Stacey, R. S., *Lancet*, 1955, **2**, 1004.

Tap-water for Injection

Q.—*May ordinary domestic tap-water, after boiling, be used in preparing solutions for injection? What are the contraindications to this practice?*

A.—It would be inadvisable to use boiled tap-water for injection. Some mains supplies may contain viable gas-gangrene spores and these may resist boiling. Tap-water may also be strongly pyrogenic. Whittet[1] has shown that a dose as low as 0.4 ml./kg. of London tap-water is sufficient to cause a mean rise in temperature of 0.59° C. on intravenous injection into rabbits. Steaming of the water for 30 minutes or filtration through a bacteria-proof filter does not prevent this effect. This response is sufficient for the sample to fail the *B.P.* pyrogen test. Man is usually more sensitive to pyrogens than is the rabbit. Tap-water is often alkaline and may contain several salts. The alkalinity or the salts may react with medicaments and inactivate them.

REFERENCE
1 Whittet, T. D., *Experiments on the Occurrence of Pyrogens in Water and their Removal and of their Pharmacology and Fate in the Body*. (London University thesis, 1958.)

Fissuring of the Finger-nails

Q.—*What is the cause of, and treatment for, longitudinal fissures which extend from the free border of the finger-nails towards the base? There is no history of trauma.*

A.—A lesion of this kind is sometimes due to trauma. It may result from a single injury to the nail matrix or nail-bed, after which the nail-plate grows in such a way as to form a fissure constantly. In some other cases the lesion may result from repeated minor trauma, such as pushing back the cuticle. In other cases a subungual lesion such as a wart or a small tumour may be identifiable. Occasionally eczematous or psoriatic nails may show this kind of lesion. There are, however, other cases where the nail-bed and matrix appear to be entirely normal and the cause of the dystrophy is obscure. Treatment is baffling.

Sahli Haemoglobin Estimations

Q.—*What is the margin of error when a competent person estimates haemoglobin by the Sahli method?*

A.—The accuracy of the Sahli method of estimating haemoglobin was determined by the Oxford group of workers during the war, and it turns out that the coefficient of variation is about 10%. That is to say, one estimation in every 20 may be expected to have an error greater than + or −20%.

These data were obtained with competent trained observers using the same standards. Some observers are quite unable to match the standard with the unknown, and some Sahli apparatus is designed in such a way that one is prevented from interchanging the position of standard and unknown; this leads to a systematic error.

The estimation of a 10% coefficient of variation is thus the minimum one for trained observers using the best apparatus under optimal conditions.

Sea-bathing and Hypertension

Q.—*Is it safe for people with moderate hypertension but normal renal function to bathe in the sea in warm weather?*

A.—There is no reason for forbidding leisurely sea-bathing to people with moderately severe uncomplicated hypertension. Diving and long-distance swims should, of course, be avoided, particularly if patients are being treated with ganglion-blocking drugs. These patients should be advised to have a companion with them in the water in view of the possible hazard caused by postural hypotension.

Asthma After Autogenous Vaccine

Q.—*A doctor, aged 36, developed severe asthma after beginning a course of autogenous vaccine prepared from a throat swab. Is this an uncommon event? Should he be desensitized with another autogenous vaccine?*

A.—It is most unusual for asthma to develop for the first time after injections of autogenous vaccine. Autogenous vaccine therapy for asthma has been shown to produce no better results than carbol-saline injections[1] and so cannot be recommended. The cause or causes of the asthma should be investigated.

REFERENCE
1 Frankland, A. W., Hughes, W. H., and Gorrill, R. H., *Brit. med. J.*, 1955, **2**, 941.

Relapse of Squint

Q.—*A boy aged 4 has a relapse of a lateral divergent squint after a successful operation when aged 2. Is a second operation likely to be successful, and when should it be done? Are there any exercises which might be successful as an alternative to operation? There is no error of refraction.*

A.—Unless the angle of squint is very small, exercises are of little value in divergent squint. There is every reason to suppose that a further operation would be successful in the case quoted, and it should be done before the child starts school.

Correction.—In the "To-day's Drugs" comment on pipamazine ("mornidine") (May 14, p. 1500) the large doses causing side-effects were given as 30–600 mg. daily instead of the correct figure 300–600 mg. daily.

Collected Articles from the "British Medical Journal"

The following books are available through booksellers or from the Publishing Manager, B.M.A. House. Prices, which include postage, are now the same for both inland and overseas.

Refresher Course for General Practitioners, Volume 3 (26s. 9d.).
Clinical Pathology in General Practice (22s. 3d.).
Any Questions?, Volume 3 (8s. 3d.).

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 4499. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.
Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs. Authors overseas should indicate on MSS. if reprints are required, as proofs are not sent abroad.
ADVERTISEMENTS should be addressed to the Advertisement Director, B.M.A. House, Tavistock Square, London, W.C.1 (hours 9 a.m. to 5 p.m.). TELEPHONE: EUSTON 4499. TELEGRAMS: *Britmedads, Westcent, London.*
MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the Association. TELEPHONE: EUSTON 4499. TELEGRAMS: *Medisecra, Westcent, London.*
B.M.A. SCOTTISH OFFICE: 7, Drumsheugh Gardens, Edinburgh.